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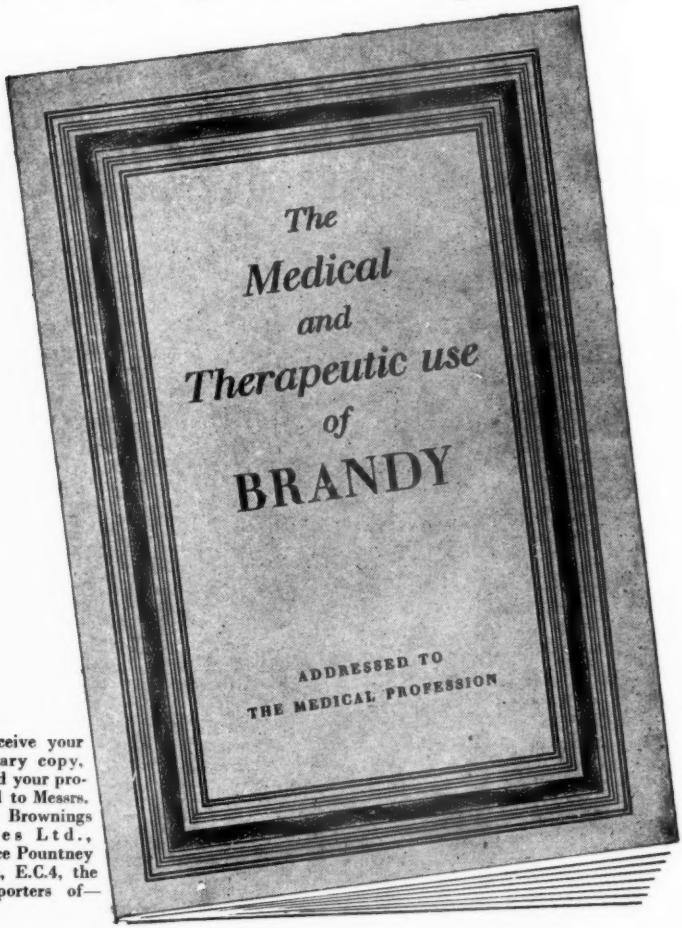

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Proceedings of the Royal Society of Medicine Vol. 48 65

Section of Physical Medicine

President—DORIS BAKER, M.D., F.R.C.P.

[*November* 10, 1954]

DISCUSSION ON PSYCHOGENIC RHEUMATISM

Dr. Desmond O'Neill: This syndrome was given the name "psychogenic rheumatism" by Boland and Corr (1943), and Philip Hench has added greatly to our understanding of the clinical picture. One of the best early papers on the subject was that by Halliday, "The concept of psychosomatic rheumatism," published in 1941. The term "tension pain" is preferable, as "psychogenic rheumatism" implies an organic disorder, which does not exist, and patients with this syndrome present themselves in departments other than those of physical medicine, such as medical or gynæcological. In a random sample of patients, recently reviewed, attending a gynæcological clinic, the commonest presenting symptom was pain, and in the great majority this was tension pain; in these women the distribution of the pain is less often "rheumatic" than abdominal.

This tension pain or sensation is distributed over a wide area, usually but not always symmetrically about the body axis. The distribution does not correspond to the picture of organic rheumatism; in some patients it is so wide as to merit the description "pain all over". The sensation is often called by the patient "burning"—a quality which is known to be associated with pain from the skin and not the deeper structures; it may also be called aching, sharp or dull, or given bizarre names. A number of patients will say that the sensation is indescribable, and the observer may have the impression that the patient is trying to convey an emotional experience rather than a pain.

The tempo of the pain is characteristic: it tends to be constant from morning to night. It may be worse when the patient is tired. The temporal correlation with stress is as a rule close; the onset and course of the disorder are related to disturbing experiences. In most patients there are other signs of emotional tension besides the pain: poor sleep, bad dreams, irritability, depression and the like. In short, the illness belongs to the category of stress disorders. The patients are usually women.

No specific personality type seems to emerge from a study of tension pain patients. One feature, however, is more common in this syndrome than in other stress disorders such as migraine and duodenal ulcer: that is, the utilization or exploitation of illness to some purpose in the patient's life. This "motivation" of the illness is kept out of consciousness to a greater or lesser degree, and it is a formidable obstacle to therapy. The pain may, for example, provide a reason for refusing to help in the care of children or to participate in sexual intercourse, or it may be employed by the patient to attract attention and sympathy from those around her. A state of pent-up anger is often present. In a recent series of 50 cases seen in the Department of Physical Medicine at University College Hospital 19 were depressed and in 4 cases the depression was severe enough to warrant electroplexy.

In this Department a special clinic exists for the diagnosis and management of tension pain. The psychiatrist works in the Department itself, and sees patients referred by his colleagues. Thus the patients do not have to be dispatched to a separate department to have psychiatric attention: there is a close and fruitful liaison between physicians, physiotherapists, and psychiatrist in the understanding and handling of the patient. The pain is recorded on a chart (a body outline printed on quarto paper), the patient being asked to mark on the chart all the kinds of pain she feels; the description

is then written beside the marking. These pain charts are invaluable as a visual record of the pain, and sometimes the chart alone, with its descriptive notes, is diagnostic. We owe the notion of the pain chart to Harold Palmer, and this device is most useful in the clinical examination of all types of pain.

The therapy of tension pain is disappointing. Some patients seem to get worse in spite of all our endeavours, and many remain quite unchanged. This failure to respond to treatment is an exception to the general rule in stress disorder, and it may be related to the meaning and purpose, already mentioned, of the pain in the patient's life.

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Dr. P. E. Sundt: I propose to discuss the words "psychogenic" and "rheumatism", but before doing so I should like to point out one cause for misunderstanding between psychiatrists and general physicians, namely the fact that most terminologies grow as a result of decaying metaphor and most of the technical terms which are used in psychiatry are metaphors which are still very much alive and therefore have no specific connotation.

The word "rheumatism" means literally a "flowing" and it was called this because it metaphorically expressed the supposed ætiology of rheumatic disorders. At the time when the name was given, about the beginning of the seventeenth century, it was so called because the rheumatic disorders were then supposed to be due to an evil humour flowing from the brain to the limbs. As this theory is three-hundred-and-fifty years old it is difficult to regard psychogenic rheumatism as a modern concept.

So far as the term "psychogenesis" goes, its increasing popularity is largely due to the unwitting obedience to the dictates of the current medical fashion, the psychosomatic concept being the successor of focal sepsis in this respect. This accounts for many mistakes in diagnosis because of the red herring of emotional conflict which can be found in anybody. The only scientific meaning of the word lies in its neurophysiological and biochemical aspects and research along these lines promises well for the future.

The great danger of the words "psychosomatic" and "psychogenic" lies in the fact that they may lead certain people to imagine that if human suffering is given a Latin name then it can be handled scientifically.

With regard to treatment three points should be considered: Firstly, in my experience it is better to give a patient a definite diagnosis rather than to attempt to give him insight, especially as the average patient, seen in a mental hospital at any rate, is not intelligent enough for psychotherapy. Secondly, the main indication for psychotherapy is the removal of secondary worries, and finally, if more patients told the whole truth about themselves a little earlier in one's acquaintance with them much of the obscurity about the causes of their depressions and tension pains would vanish.

Dr. Ernest Fletcher and **Dr. J. H. Jacobs:**

Dr. Fletcher delivered the Address as follows: To discuss the problem of psychogenic rheumatism without mentioning psychiatry is rather like singing a song without words, but I should like to approach this subject primarily from the point of view of a physician interested in the rheumatic disorders who is faced with the problem of diagnosis and treatment of these painful locomotor manifestations of a disordered emotional state. I do not intend to delve into the realms of psychopathology or personality types.

Psychogenic rheumatism may be defined as the musculoskeletal expression of functional disorders, tension states, or psychoneuroses, but I exclude from this category the concept of organic joint disease of psychosomatic origin.

The term psychogenic rheumatism has met with much opposition on the grounds that rheumatism implies some primary organic tissue change; however, although scientifically inaccurate, it is a conveniently comprehensive description when one realises that the very addition of the word psychogenic postulates that emotions may bring about somatic disturbances, including subjective symptoms of pain and stiffness, and many cases diagnosed as nonarticular rheumatism can be understood and interpreted in terms of psychoneurotic concepts.

The recognition and disposal of these cases of psychogenic rheumatism represents both an economic and a medical problem. Halliday (1941) when acting as a medical referee in Scotland found that 39% of 145 consecutive patients seeking insurance benefit who were labelled rheumatism were, in fact, incapacitated by reason of psychoneurotic disorders; this incidence was considerably higher when only those cases off work for two months or more were considered. During periods of great

stress, such as wartime, it is not surprising that the increase in emotional conflicts gives rise to a subsequent increase in somatic manifestations. Boland and Corr (1943) in the U.S.A. found that psychogenic rheumatism was the most frequent cause of disability in soldiers with rheumatic complaints who were admitted to army hospitals: they found this to be so in 34% of 450 consecutive admissions, many of these patients having previously been given organic diagnoses. Flind and Barber (1945) reported that 42% of patients admitted to a Royal Air Force special rheumatism centre were suffering from psychoneurotic disorders.

The incidence of this disorder in rheumatism clinics varies with the care and accuracy taken in diagnosis and the source from whence these patients come, such cases seldom slipping past an interested G.P. who, with his knowledge of the patients' background, is probably better equipped to deal with their problems than the rheumatologist or psychiatrist. During the past year the incidence of primary psychogenic rheumatism found in the Royal Free Hospital Unit of Rheumatology was less than 4%, although the occurrence of a considerable functional overlay in patients with minimal disease was higher. Rheumatologists may obtain some satisfaction when they realize that they only handle small numbers of these patients, and that psychiatrists probably see many more patients complaining of somatic pains arising from mental tension than are seen in our own out-patient departments. Edmonds (1947) found in 183 adults suffering from psychoneurosis that 87 (47%) suffered from pains referable to the locomotor system.

However, every department has its quota of misdiagnoses, functional disease being diagnosed as organic and vice versa; we all feel a certain satisfaction when on reviewing these cases we label such patients as psychoneurotics, but no doubt the psychiatrists obtain even greater satisfaction when they discover that patients referred to them with the diagnosis of psychogenic rheumatism have, in fact, organic disease, especially as this error may well be made in patients who have some degree of secondary functional overlay.

While most clinicians agree that the over-investigation of patients suspected of suffering from psychogenic rheumatism may be harmful in potentiating and fixing attention on the somatic aspect of their disease, failure to carry out thorough clinical and basic radiological and pathological examinations can lead one into greater difficulties. Firstly, the patient considers he is being neglected, and therefore becomes more resentful and difficult to handle, and secondly, there are certain organic diseases whose symptoms are closely simulated by those of psychogenic rheumatism and which may be missed in the absence of adequate radiological investigations.

There are the vague aches and pains which occur in the early stages of ankylosing spondylitis. I have at present 2 patients who were considered to be psychoneurotics during their Service careers, one of whom was actually forcibly removed from his bunk on to the parade ground during an acute attack of sciatic pain and threatened with disciplinary proceedings: after this episode it is not surprising that he never again reported sick although his back became gradually stiffer. Perhaps it is understandable that such cases may be missed when one realizes that the average time between the onset of the symptoms of ankylosing spondylitis and the diagnosis of the disease in my experience is about four years.

Pain arising from bone may be another diagnostic pitfall. Osteoporosis of the spine, fibrocystic disease, and at times myelomatosis and unsuspected carcinomatosis frequently present with no obvious physical signs and may be labelled functional in origin in the absence of adequate investigations.

At times the symptoms of cervical spondylosis may appear to be bizarre in character: pain radiating up the neck, over the occiput and felt at the back of the eyes associated with headaches, such as occur in the "posterior cervical syndrome", may well be considered psychoneurotic in origin, especially when associated with vague pains over the upper dorsal area and pain across the chest typical of a pseudo-anginal state.

Neurological conditions may be another source of misdiagnoses—peripheral neuropathy, shoulder girdle neuritis of the type described by Spillane (1943) and tumours of the cord and cauda equina.

I would like to mention a case where both the original clinicians and psychiatrists were equally misled.

A girl aged 15 was brought to a rheumatic clinic by her despairing parents with the history of pains in her back and legs since the birth of their second child five years previously. This pain was at first associated with a limp which had since developed into a bizarre gait. She had been under the care of an orthopædic surgeon from the onset of her pains, and since no cause for these was discoverable, and as she had developed this peculiar gait, she was referred to a child psychiatrist. Her psychiatric history even at the age of 12 ran to six foolscap pages, and it was hard to believe that one so young could have experienced so many unusual emotions, phobias and conflicts—it appeared that she was a psychoneurotic of the worst order. Examination revealed a sulky, suspicious girl with a gait that was hard to describe in any anatomical terms. The only abnormality discovered, apart from her gait, was one slightly diminished knee-jerk. The case was discussed with the neurologists and a myelogram revealed the presence of a space-occupying lesion in the spinal canal. This proved to be a neurofibroma, and following operation her pains disappeared and her walking improved.

Whether her gait was in fact entirely due to her lesion or to a superimposed psychoneurosis is a matter of conjecture, but diagnoses may be so difficult at times that even the combined efforts of the clinician and psychiatrist may fail to arrive at the truth.

Returning briefly to the other side of the question—the diagnosing of the organic for the functional—perhaps we have ourselves to blame for so easily accepting the term "primary fibrositis". It is, admittedly, an attractive diagnosis, well understood by the patient and respectable enough to be discussed over the bridge table. The tendency therefore to temporize with this diagnosis is not always suppressed by the physician, and the patients are given an organic label which satisfies them, and at the same time absolves the doctor from further diagnostic worries. This type of patient, in whom the disease has already been potentiated, is all too often met with, and any efforts to convince them that their symptoms are psychogenic in origin are met with a withering superior smile, for have not Dr. A., Dr. B., and Drs. X, Y and Z already told them that they suffer from fibrositis for which, as everybody knows (except the clinician in question), the cure is prolonged physiotherapy—preferably of a passive and pleasant nature.

On what grounds can we therefore base our diagnosis of psychogenic rheumatism? Firstly, by the exclusion of organic disease; this decision must be reached promptly for, as Weiss (1947) points out, unless this is so then the "physician becomes a pathogenic agent in perpetuating the illness by his well-meaning but never-ending efforts to find a physical cause." Secondly, by the recognition of psychoneurotic traits; Boland (1947) has suggested three criteria for this: (1) a psychoneurotic predisposition, (2) emotional conflict and (3) restriction of outward expression. However, the recognition of all these traits probably sets a very high psychiatric standard for physicians to follow, with the limited time at their disposal, especially as the motivation of the symptoms may well be hidden from the patients themselves.

Clinically it is helpful to divide psychogenic rheumatism into three subtypes: (1) somatic manifestations arising from primary emotional conflict, (2) similar manifestations superimposed on organic disease, and (3) perpetuation of somatic symptoms.

I do not intend to go into great detail regarding the history, symptoms, and signs as we are all familiar with the tense or depressed individuals who sit on the edge of the chair and are prepared and determined to tell you their history from its very onset. Certain points, however, stand out. The length of history is usually very vague and on being asked how long have they felt their pains the most frequent reply is "ever since I can remember, doctor"; although at times they are able to relate the onset of their disability to some specific emotional stress and may also be able to associate exacerbations of their symptoms with further periods of mental conflict. Frequently their pains are diminished when on holiday or when they are removed or protected from difficult situations. A history of other associated diseases or symptoms is frequently obtained—peptic ulcers, colitis, dysmenorrhœa, effort syndrome, nervous breakdowns and headaches being among the most common. The elucidation of an accurate family history is often very helpful: a history of cancer, arthritis, or crippledom of any type may be given and at this point a direct question to the patient of "are you worried that you have the same trouble?" is often answered in the affirmative.

The pains are usually diffuse in distribution and systemically difficult to relate, or they may tend to be more localized over one area, such as the lower part of the spine. They are described in a variety of graphic terms from agonizing to aching, burning, pricking, perpetually sore, and so on.

Other concomitant symptoms, such as loss of weight, anorexia, sleeplessness and morning tiredness are invariably obtained.

Apart from the general signs of anxiety, tremor, sweating, increased reflexes and flinching on examination, abnormal signs in the locomotor system are limited to muscle spasm which may be so severe at times as to cause apparent fixation of the back or limitation of joint movement. Holmes and Wolff (1950), using needle electrodes, have shown that there is a sustained increase in motor and electrical activity in these patients.

The second type, in which psychogenic symptoms are superimposed on organic disease, is perhaps more commonly encountered. Usually these patients have minimal disease—Heberden's nodes, cervical spondylosis, or creaking joints with slight pain at times. Over these patients the fear of crippledom hangs heavily, they become anxious and tense, and so develop secondary somatic pains; simple reassurance in this type of psychogenic rheumatism should be tried and is frequently effective.

Difficulties may arise in diagnosis with this subtype, as illustrated by the following history:

A man aged 19 had suffered vague pains since the age of 14; he had been unable to compete with his fellows at school and took consolation in overeating and became obese. He was mocked at for his inability to run and for his obesity. His pains continued, and at the age of 19 ankylosing spondylitis was diagnosed. When he was admitted to the wards for deep X-ray therapy he was tense, anxious and resentful. Gradually both the organic and functional aspects of his disease were explained to him, an explanation he gladly accepted, and before his course of therapy was half completed much of his symptomatology had already disappeared and there was a considerable improvement in his mental outlook.

One can speculate that the third type of psychogenic rheumatism, the residual, with perpetuation of somatic symptoms, can arise in two ways. Although muscle tension is at first a result of mental conflict, it may become perpetuated as a habit which long outlives its original cause. Frequently one sees such patients who have long come to terms with themselves and whose mental conflicts appear to have been resolved, but who continue to suffer with their pains. We should try to differentiate this type of patient from those who have built their lives around their symptoms and in whom too vigorous interference may precipitate further psychogenic manifestations. On the other hand, as Elliott (1944) suggests, the sustained contraction of muscle may impede intramuscular circulation with subsequent fibrosis. The type of backache following disc lesions or "railway spines" may result from this cause. Thus it is possible that pains commencing as somatic manifestations of a functional disorder may ultimately become organic and irreversible in character.

The treatment and disposal of these cases from the point of view of a rheumatologist present many problems.

The first essential is to come to a firm diagnosis and to endeavour to explain rationally the nature of his illness and his syptoms to the patient. It is useless merely to tell him that he suffers from nerves, or to reassure him that there is nothing wrong with him when the patient is experiencing abnormal sensations which he knows normal people do not experience—to persevere with this line of treatment is merely to make the patient more resentful and antagonistic.

How far into the psychoneurotic aspect is it wise for those of us with limited psychiatric knowledge to go? This must of course depend on experience, interest and time at one's disposal. I believe, if time permits, that one should try with simple rationalization to help the early cases of anxiety, as frequently some obvious worry, resolvable or otherwise, may be to the forefront of their mind, which the patient is only too anxious to discuss, but I realize that here I am on dangerous ground as the differential diagnosis between anxiety and hysteria is not always easy to make. The depressed, the obsessionals, and the hysterics are certainly best left to our wiser psychiatrist colleagues, for in order to help this type of psychoneurosis, specialized knowledge and techniques are essential.

From the physical medicine point of view, progressive relaxation as an aid to psychiatric treatment may at times be helpful, provided that the patient understands its aims and is in a receptive state of mind.

In the past, failure to recognize this type of illness has led to many irreversible cases of tension states and the application of much wasted physiotherapy. However, with better realization of the mechanism of these pains perhaps this discarded pool of unfortunate chronics will dry up and cease to haunt our departments.

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Dr. **William Tegner:** I am one of those who believe that I am occasionally asked to see patients who have been diagnosed as suffering from rheumatism, but who, in my opinion, are in fact suffering from illness not of the body but of the soul.

Psychogenic rheumatism appears to arise in three ways. (1) It may be merely an exaggeration of the symptoms of organic disease. This exaggeration may be so extreme that the hysterical symptoms become completely predominant and bury the symptoms of the underlying disease. Nevertheless, there is here underlying organic disease which it is the duty of the diagnostician to discover and treat. (2) Psychogenic rheumatism may arise as a prolongation of symptoms of an organic disease which is long past and done with. This is a common condition. (3) We meet patients whose symptoms are entirely psychogenic, and in no way related to organic disease. These patients have chosen rheumatism as a protection against the difficulties of life. It is the last two of these three types which I think present us with the greatest of our problems.

Why do patients pick on "rheumatism"? Why does the psyche choose this barrier against its difficulties? There are many reasons for this. Firstly there is fear, for a relative may have been crippled with rheumatoid arthritis. Then rheumatism is a vague and ill-defined term. It is the patient, not the doctor, who uses the phrase "only rheumatism". This leads to the second reason for the

choice of rheumatism by the patient's subconscious mind, for to the lay mind rheumatism, while common, is not fatal. A recent investigation into public opinion on cancer by Paterson and Aitken-Swan (1954) showed that rheumatism was the least feared of a group of conditions, including cancer, tuberculosis and heart trouble. The sufferer from "rheumatism" usually gets sympathy and support, and "rheumatism" has the reputation of being a lengthy business, with frequent exacerbations which can often arise at a suitable moment to help in the escape from an urgent difficulty. Then again, rheumatism is traditionally treated by physical methods which may mean frequent attendance at clinic or hospital, attendance which necessitates the abandoning of any other job or activity. Such attendance at hospital or clinic enormously increases the patient's importance in her own eyes, in her employer's eyes, and in the eyes of her family. No wonder rheumatism is a safe and pleasant protection for the agitated or inadequate personality.

The diagnosis of psychogenic rheumatism is fraught with difficulty. It cannot be used as a refuge when we cannot find any physical signs; no more are we justified in shrugging our shoulders and saying: "... must be psychogenic" when treatment fails to achieve the expected cure. But the sufferer from this type of disease often gives herself away by her vague history, full of irrelevances and exaggerations; her pain does not fit in with human anatomy, and, on examination, she is tense and demonstrative. Such an attitude leads us to investigate further, and see if a diagnosis of psychogenic rheumatism can finally be justified.

The management of the patient suffering from psychogenic rheumatism is one of the most difficult problems that one can meet. Fundamentally, the patient's symptoms are useful to her, and she is reluctant to lose them.

It would appear that if psychogenic rheumatism is a form of hysteria, the psychiatrist should be responsible for the treatment of the patient. But quite apart from the fact that the patient is usually very reluctant to accept the diagnosis that her troubles are not organic, and to be persuaded to consult the psychiatrist, the psychiatrist himself is up against the problem of dealing with an inadequate personality, who is unwilling to abandon such useful and profitable symptoms. The psychiatrist is tempted to say that the inadequacy of the patient was established in childhood, and that it is now too late to do anything about it. A neurologist, experienced in the handling of hysterics, once told me that it was a mistake to try to remove a useful psychogenic malady from the patients as they would inevitably revert to something else, and it would be even harder to manage.

Many of the patients are referred for physical treatment, and expect it. Fundamentally this would appear wrong, for it does not seem right to treat a non-organic disease by physical means. But these patients are sent by psychiatrists and by general practitioners, who ask for "suggestive treatment" or some such phrase. Under the treatment the patients seem quite contented, but are never cured. If, after prolonged treatment, they are discharged with the explanation that treatment does not seem to be of any value in their case, the patients always seem to badger the general practitioners to be sent back for more treatment, as it is the "only thing that has kept them going". If the physical treatment which they are given is uncomfortable they clamour that it is making them worse, and that they want some other treatment which they have had before, or think they have seen other patients receiving. They are great believers in lying on a couch and being massaged.

What, then, is the solution to this problem? What can be done about these patients who, in turn, exhaust general practitioners, consultants, psychiatrists and physiotherapists? The answer is nothing; they will always be with us, and the burden must be shared in turn by all the team.

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Section of Surgery

President—HAROLD C. EDWARDS, C.B.E., M.S., F.R.C.S.

[*November* 3, 1954]

DISCUSSION ON TREATMENT OF MALIGNANT DISEASE OF THE UPPER JAW

Mr. A. J. Gardham:

Surgeons who treat malignant growths in the mouth and pharynx must look forward to having at least two failures to every one success and my own survey of the end-results of carcinoma of the upper jaw suggests that if the growth originates in the nasal sinuses the cure rate is even lower. Thus, in considering this disease, there is very good reason for looking at treatment from the point of view of the uncured as well as the cured.

When one sets out to treat a patient with a growth in the upper food or air passages certain considerations must be taken into account. They are:

(1) The chances of cure. (2) The penalty which the patient pays for an attempt at cure. (3) The duration of life in uncured cases. (4) The possibility of making the remainder of the patient's life more tolerable by palliation.

Considering these points in relation to carcinoma of the upper jaw originating in the nasal sinuses, the answers appear to me to be as follows:

(1) The chances of permanent cure are low and therefore the other considerations count for more when treatment is planned than they do when one is dealing with growths of lower malignancy.

(2) The penalties of any attempt at radical cure are very considerable if the attempt involves a major excision. An unsuccessful attempt which opens up large areas of raw tissue involves a very real risk of diffuse recurrence in the wound bed. This risk must not be incurred lightly as it certainly leaves the patient worse than he would have been with an untreated growth. The penalties of more limited operations are much less whether they succeed or fail.

(3) The average duration of life in uncured cases is well below a year in the series which I have studied but survival for three or four years is not uncommon. Thus, the quality of life which we can offer to our patients when the growth is not cured is very important.

(4) *The possibility of palliation.*—The worst features of untreated and uncured growths are pain and foul discharges. Neither of these is an essential part of the picture of a growth in the mouth. Pain is generally due to one of three things: Invasion of compact bone, very extensive invasion of soft tissues, or sepsis. In the antrum sepsis often accounts for a large part of the pain and if sepsis is controlled by diminishing the extent of the growth and providing free drainage pain is greatly diminished. The same is true of discharge. Invasion of compact bone is rare in growths originating in the nasal sinuses and the danger of producing massive necrosis of bone by irradiation is much less than it is, for instance, in a carcinoma of the floor of the mouth. Thus, in growths of the upper jaw palliation by drainage to relieve sepsis and careful irradiation to diminish the size of the growth is well worth while even if it does not produce a cure.

Available methods of treatment.—The classical excision of the upper jaw is rarely indicated in growths which originate in the nasal sinuses. In these growths it produces few cures. Its penalties are high and it gives palliative results which are no better than those produced by some of the more restricted operations combined with irradiation. The operation gives good results in growths originating in the alveolus and palate or in the mucous membrane of the mouth and in these cases can be modified in such a way that it produces little permanent deformity.

Thus, for growths originating in the nasal sinuses I think the technique of restricted operation combined with irradiation is right provided that we accept the present cure rate as the best which we can manage.

We ought, however, to consider possible lines of advance. These are: (1) Extension of the classical operation to make it truly radical, and (2) The application of radical surgery directly it is clear that the original operation of access and irradiation has failed to cure the growth completely.

Every surgeon who has performed a classical excision of the upper jaw for a growth originating in the nasal sinuses knows that it is an unsatisfactory technical procedure as it does not conform with the ordinary requirements of an operation for malignant disease. These requirements are that the growth itself should be in the centre of a sphere of tissue with an adequate margin of apparently normal tissue at the periphery. In the classical operation the margin is very small posteriorly, and to make it really satisfactory the operation must be extended backwards, upwards, and towards the mid-line. This can only be done by removing the ascending ramus of the lower jaw together with the pterygoid muscles and the pterygoid plates, displacing the lateral wall of the pharynx and the common carotid artery and exposing the base of the skull. In most cases it involves removing the lateral mass of the ethmoid and clearing the orbit. An operation of this type was a very difficult surgical feat until the introduction of the very modern forms of anæsthesia which make use of hexylmethonium compounds to reduce bleeding to a minimum. With these compounds the operation is simple but risky. It is too soon to say how much hope it gives but there is not much room for

optimism because the post-mortem records of patients who die within a year of their first consultation show that nearly half of them have distant metastases well developed when they die, and probably had the seeds of metastases when they first sought advice. The other possible line of advance which appeals to me strongly is to apply radical surgery more freely in cases in which there is residual growth after an operation for access and drainage and a single irradiation. I do not think there is much to be expected of this unless the more radical operation of which I have spoken is adopted but if the results in other parts of the mouth are any guide second and third irradiations very seldom produce a cure and there is much to be said for employing a truly radical operation once it is clear that the original irradiation has failed to arrest the growth completely. My guess is that the adoption of this principle together with the extended operation would result in some improvement in the survival rate but the improvement would not be very great because of the frequency of distant metastases.

There are two other points to which I wish to refer. The first is the place of microscopy in assessing prognosis and determining the appropriate treatment. I am sure that it is of some value but I believe that this value is often exaggerated and I must confess that I have found it of very little help except in demonstrating invasion of glands. On the other hand the site of the growth and its macroscopic appearances are sometimes very helpful indeed. There is a type of growth which behaves very like the nasopharyngeal growth which is now so well recognized, in that it spreads submucously, does not ulcerate and is very radiosensitive. (An illustration of such a case is given in Gardham, 1939, *Lancet*, i, 677.) These growths produce enlargement of the upper jaw but they are distinguishable from antral growths because pain is much less and discharge and fœtor are absent. Biopsy is just as difficult and unsatisfactory as it is in the nasopharyngeal growths but tele-irradiation produces quick regression of the tumour though remote recurrences are the rule. Growths of the upper jaw which originate in the palate or alveolus generally conform to one of two types. There is the papillary exfoliative growth which spreads widely but superficially and gives surprisingly good results with surgery. There is another type of growth which starts in the alveolus leaving a very small ulcer on the surface with none of the classical signs of malignancy but invades the bone deeply and widely. This latter type is commoner in the lower jaw, but it is important to recognize it as it does not show the ordinary clinical appearances of a carcinoma but nevertheless invades the bone very deeply and widely and requires a correspondingly extensive excision.

The extent of the residual deformity which is to be expected after the extended operation is shown in Fig. 301 (C and D) in Gardham, 1953, *Brit. J. Surg.*, **41**, 249. This patient had a very big growth which did not originate in the antrum and it was possible to leave the ethmoid and the orbital plate sparing the eye. The right half of the lower jaw, the pterygoids, the whole of the right upper jaw with the exception of the orbital plate and part of the left upper jaw were removed. As the figure shows the deformity is marked but it is by no means intolerable and four years after operation this patient, who is now 83 years old, is able to eat well, talk volubly and smoke to excess and is correspondingly happy.

Mr. C. P. Wilson: I propose to restrict my remarks to growths arising primarily in the antra and anterior ethmoidal regions.

Both surgery and radiotherapy have been used independently, but most workers agree that the best results are obtained by a combination of the two. Complete surgical extirpation is limited to small growths commencing on the alveolus or in a tooth socket. Such early cases are not numerous and can be dealt with by an operation of less extent than the formal operation for excision of the upper jaw. I do not think that this classical operation has any place in modern treatment.

Insertion of radium needles into the centre of the growth has occasionally produced cure but it is impossible to obtain a homogeneous distribution of dosage by such a method and successful results have usually been obtained at the expense of extensive necrosis of surrounding bone. External irradiation by teleradium or high voltage X-rays is more satisfactory as a homogeneous distribution can be more easily obtained but after treatment is completed necrosis is common because of associated sepsis: nor is it possible to decide whether or not the tumour has been completely destroyed, nor can recurrence be detected until it has reached formidable proportions.

It was to remove these disadvantages that it was decided that treatment must be a combination of surgery and radiotherapy.

Removal of a piece of tissue may be necessary to make certain of the diagnosis before treatment is commenced and this can be taken from suspicious tissue in the ethmoidal region or from the cavity of the antrum through the canine fossa. If the diagnosis is not in doubt it is better to defer taking a specimen until after treatment has commenced.

If there is marked infection of the antrum then drainage should be undertaken at the same time as the biopsy. Drainage is most useful intranasally. A large portion of the inferior turbinate is removed and a large opening made into the antrum through the lateral nasal wall using a bent diathermy electrode—the straight part of the electrode being covered with capillary tubing.

A full course of external irradiation is then given. Both teleradium and deep X-rays have been used at the Middlesex Hospital. With the former a 4-gram unit and later a 10-gram unit; X-rays

have been used with a conventional 200 kV apparatus. There does not seem to be a great deal of difference in the results obtained but the risk of necrosis in cases of gross sepsis is possibly less with teleradium. The dose given varies from 4,500 r to 6,000 or 7,000 r and according to the histological type of growth over a period of four to seven weeks; an average dose over the whole period of roughly 1,000 r per week using a five-day week. Each patient is planned individually and for the planning to be properly undertaken it is essential for as accurate a localization of the anatomical site and extent of the disease as possible to be provided by the clinicians—the surgeon and radiotherapist in combination.

During the late stages of irradiation there are generally obvious and visible signs of regression of the tumour—swelling of the cheeks gets less, proptosis is less marked and the nasal airway improves. This improvement continues for some few weeks after treatment has finished with absorption or discharge of necrotic growth and resolution of the accompanying swelling. By the end of four to six weeks the major part of the inflammatory reaction following treatment has subsided.

The next step is the most important one. Its object is to provide a permanent window for future inspection, to destroy any remaining neoplasm and to provide a large single cavity for possible future treatment. Intratracheal anæsthesia is used with a tube passed through the opposite nostril and the pharynx securely packed off. The patient is placed in a semi-sitting position with the head thrown back. Top lighting is sufficient for the first half of the operation but a head lamp is usually necessary for subsequent stages. Two silk stitches passed through the lip; one in the middle line and the other at the angle of the mouth make very convenient retractors.

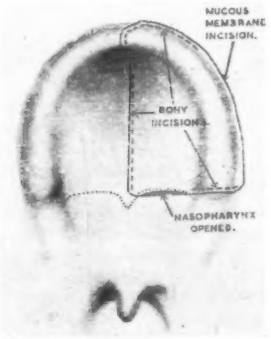


FIG. 1.

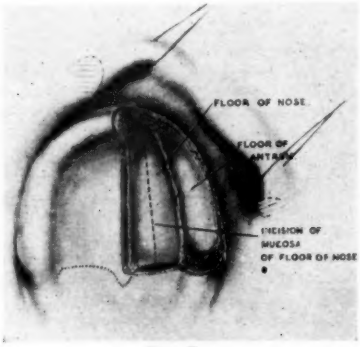


FIG. 2.

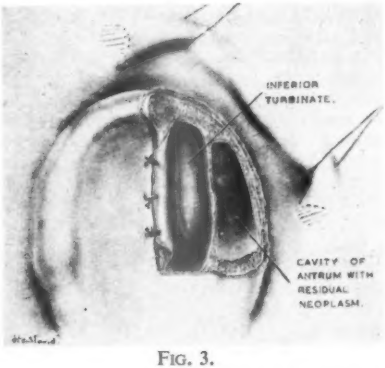


FIG. 3.

FIG. 1.—Shows the lines of the incisions in the mucous membrane and the lines of bone division.

FIG. 2.—Shows the appearance after removal of the bony floor of the nose and antrum.

FIG. 3.—The antrum has been opened and the mucosa of floor of nose sutured to the mucosal edge of the hard palate.

FIGS. 1–3 are reproduced from WILSON, C. P., 1954, *Ann. R. Coll. Surg., Engl.*, **14**, 285, by kind permission.

The first step in the operation is to outline a triangular area, the sides of which are respectively the middle line of the hard palate, a transverse line passing from the posterior end of this incision to the outer side of the alveolus behind the last molar tooth but just in front of the tuberosity and the third line joins these two incisions in the alveolar sulcus (Fig. 1). A diathermy needle is used for this with a cutting current. The posterior transverse incision usually opens up branches of the posterior palatine vessels with free bleeding; this is easily dealt with by applying a fine sucker to the bleeding area and using a coagulating current. At its medial end the incision passes down to the spine of the hard palate

in the middle line while at its lateral end it passes over the posterior part of the alveolus. In the middle part it divides the hard palate from the soft palate and enters the nasopharynx.

The bone is divided by an osteotome just to the side of the middle line and splits the alveolus anteriorly and then the hard palate. The posterior end of the alveolus is then divided in the line of the transverse incision. A blow with a wide gouge in the region of the canine fossa enables the whole of the alveolus and palate to be levered off exposing the mucous membrane of the floor of the nose and also the mucosa of the floor of the antrum. The canal of the posterior palatine vessels is opened up with this removal of bone and there is free bleeding from the vessels. This is easily controlled by coagulation with the electrode pushed into the canal. More bone is now removed with a gouge from the incisor region so as to expose the floor of the nose as far forwards as possible and the rough edges of the hard palate nibbled away as far as the middle line (Fig. 2).

The mucous membrane of the floor of the nose is now divided from before backwards about $\frac{3}{8}$ in. from the middle line and the lateral part removed with the diathermy as far as the antronasal wall. The medial part of the mucous membrane of the floor of the nose is sutured with two or three catgut stitches to the mucous membrane of the hard palate in the middle line (Fig. 3). This hastens healing and makes subsequent insertion of an intracavitary applicator much less uncomfortable for the patient. The antrum is opened by removal of the mucous membrane forming its floor and the nasal and antral cavities can now be inspected. It is convenient to place gauze strips moistened with cocaine and adrenaline into the upper parts of the cavities.

The inferior turbinate and remainder of the antro-nasal wall are removed with a bent diathermy needle as far up as the middle turbinate. As much of the bone of the anterior and lateral walls of the antrum as possible is now also removed and specimens of tissue taken from any areas originally affected by growth for microscopic examination. The middle turbinate and ethmoidal block is removed as far as possible in one piece and also sent for examination. If the original growth is in the antro-ethmoidal region or on the posterior wall of the antrum the posterior ethmoids should be exenterated and the sphenoid opened, even if no growth is apparent in the ethmoidal region. If there has previously been erosion of the orbital floor this should be removed also but the orbital edge is left unless it is definitely involved. Similarly as much of the inner wall of the orbit as practicable is removed especially if previous invasion of the orbit exists.

Up to this point a cutting current is used but now all doubtful areas remaining are coagulated as thoroughly as possible, care being taken to avoid the optic foramen. Any bleeding vessels are coagulated but it is not often that bleeding causes any serious inconvenience. The cavity is sprayed with penicillin and sulphathiazole powder and a previously prepared plastic obturator of very light construction inserted. There is no dressing or plugging. Penicillin is given for a week after operation. Modifications of this general scheme can be made.

If the growth is alveolar or buccal there is no need to do such extensive exenteration of the ethmoids and orbital walls as has been described and even the middle turbinate can be left, while in cases involving the posterior part of the antrum the whole of the tuberosity and even part of the soft palate adjoining it may need to be removed. In some cases, particularly if the antero-superior wall is involved with invasion of the orbit, it may be necessary to reflect the cheek using a modified Moure's incision so as to remove the whole anterior wall of the antrum including the orbital edge. The simple light obturator is removed after each meal and the cavity irrigated with weak sodium hypochlorite solution. Pain is not as a rule very severe and can usually be controlled with aspirin. I have not had any serious reactionary bleeding although there is usually œdema of the cheek for a week or two. When the œdema has subsided the obturator is replaced by a new one fitted with a small flange; this is more comfortable and more easily retained in position. A permanent obturator with teeth is not fitted for at least three months after operation. If the material removed at operation does not show any growth, and this was the case in some 30% of cases, nothing further is done but the patient is watched carefully at monthly intervals for a year and subsequently at longer intervals.

The most annoying complication is that of sequestrum formation, particularly in the zygomatic region and in the region of the tuberosity of the palate. Such sequestra may take many months to separate but do not necessarily cause any symptoms, and need not be interfered with. Originally, patients were occasionally lost from meningeal and pulmonary complications but with the routine use of antibiotics during the last ten years such complications have been rare.

The most serious complication of the treatment as a whole is the development of cataract in the eye on the affected side and this slowly develops during the course of the first two years after treatment.

If growth is found to be still present at operation or in the microscopic sections of tissue removed at operation then radium is applied by means of an applicator moulded into the cavity. A hollow applicator fitting the cavity is made by the dental surgeon of vulcanite or other plastic material. The applicator is filled with wax and drilled to take the radium tubes. The position of these tubes varies according to the areas of persistent growth and to the size and shape of the cavity and is worked out by the physicist to produce a dose rate on the surface of the mould of about 70–100 r per hour giving a dose of 6,000 r in 60–90 hours. The falling off of the dosage rate from the surface of the mould is very rapid so that the applicator cannot be considered as providing anything more than surface treatment in the cavity but if the coagulation has been efficient this is all that is required.

if, however, there is spread to the posterior ethmoidal or sphenoidal regions it is necessary to insert radium needles into those areas. Each case must obviously at this stage be planned individually just as was the original treatment.

If at the original planning there is no evidence of metastasis in the glands of the neck no treatment need be given to the neck but if there is evidence of glandular involvement then irradiation is carried out to the glands at the same time as the primary lesion is treated. I do not think that block dissection of the neck should be undertaken primarily. The glands likely to be first involved are those high up on the lateral pharyngeal wall and these are not amenable to removal in a block dissection. Dissection of glands is carried out in cases where localized glandular enlargement persists after the completion of the radiotherapy treatment of the primary lesion and glandular field.

Some workers consider that surgical extirpation of the growth should be attempted in the first place and that irradiation should be given subsequent to operation. At the Middlesex Hospital my radiotherapeutic colleagues and I begin with a full course of external irradiation as the first procedure and then, if necessary, give post-operative irradiation by radium inserted into the cavity. We prefer this sequence as we consider that pre-operative irradiation is more effective, and that the tumour is usually more radiosensitive when it is irradiated with its blood supply unimpaired by previous surgical interference. Possibly also there may be less chance of dissemination of neoplasm as the result of operation if a full course of irradiation has been given beforehand. For the same reason I do not take a biopsy in those cases where the diagnosis is certain until about 1,000 r of radiation has been given. I have found that in more than one-third of the cases there has been no growth discernible histologically in the material removed at operation after irradiation.

Many cases do not present themselves for treatment until a very advanced stage but it is surprising how often successful results were obtained, and I do not consider this to be a contra-indication to treatment. A more common cause of failure is the poor general condition of a patient with an advanced growth and prolonged sepsis which prevents adequate treatment. Local recurrence most often occurs with growths invading the posterior wall of the antrum and extending into the pterygoid regions. The tragedy of such cases is that they have often had symptoms unrecognized for many months before diagnosis is made.

Growths invading the ethmoidal regions and the orbit are a most difficult problem and the results of treatment of such cases are very poor. Although every possible attempt is made to protect the eye on the opposite side the eye on the affected side is ignored and this may result in subsequent cataract and may even necessitate removal. It is the desire to protect the eye or orbital contents on the affected side which so often prevents efficient coagulation in the ethmoidal and orbital areas and I feel that in cases of this nature exenteration of the orbit should probably be carried out at the time of the palatal antrostomy. Unfortunately, it is difficult to persuade a patient that the eye should be removed if there is good vision present, even though it has to be kept covered and cannot be used effectively because of diplopia. It is quite impossible to persuade a patient to submit to this if his vision is good and he can use the eye, nor is it easy for the clinician to realize that the loss of the eye may make the difference between success and failure. It is possible that with the development of newer methods of treatment such as the convergent beam technique and the cobalt 60 bomb with their ability to produce a more powerful and more localized depth dosage this problem will be overcome.

The results of treatment by the methods described are definitely encouraging. Of 171 cases seen up to 1950, 151 were treated. In the period up to 1937 there were 14·7% three-year cures and 11·8% five-year cures. In the following ten-year period (1938–48), there were 33·8% three-year cures and 23·1% five-year cures. For the years 1949 and 1950 the three-year cures were 72·7%.

I do not wish to stress this last figure, which only refers to a three-year cure period, but results have steadily improved with each period and I feel there is every reason for encouragement.

Mr. Alan H. Hunt: The unanimity of opinion that exists between Mr. Gardham, Mr. Wilson and myself is largely that of dissatisfaction at the results of treatment.

Squamous cell carcinomata of the antrum.—To add emphasis to this point, Dr. M. Lederman has kindly allowed me to quote his and Mr. W. A. Mill's results of radiotherapy combined with surgery at the old Cancer Hospital (now happily re-named the Royal Marsden Hospital after its founder). Out of 239 cases of upper jaw cancer, 112 were antral tumours and of these 87 (or 78%) were squamous cell carcinomata. This is the largest and most difficult group to treat. The five-year recurrence-free survival rate (to 1952) is no more than 34%. Capps and Williams (1950) gave 34·5% for a comparable though smaller series of similar tumours at St. Bartholomew's Hospital.

The corresponding figure for the non-squamous tumours is 43%.

Initial planned treatment.—At both St. Bartholomew's and the Royal Marsden Hospitals the treatment has been similar—high voltage therapy in the first place followed by surgical excision of the residual tumour and full exposure by removal of the palate and alveolus, the operative approach being from within the mouth. The lymphatic glands, when they are involved, are treated by block dissection or high voltage therapy, depending upon whether the glands are mobile or fixed. The glands have not been commonly involved.

Recurrences.—Recurrences are treated by intracavitary irradiation or radical excision. My own experience with the radical operation has shown that it can be successful after all other methods have

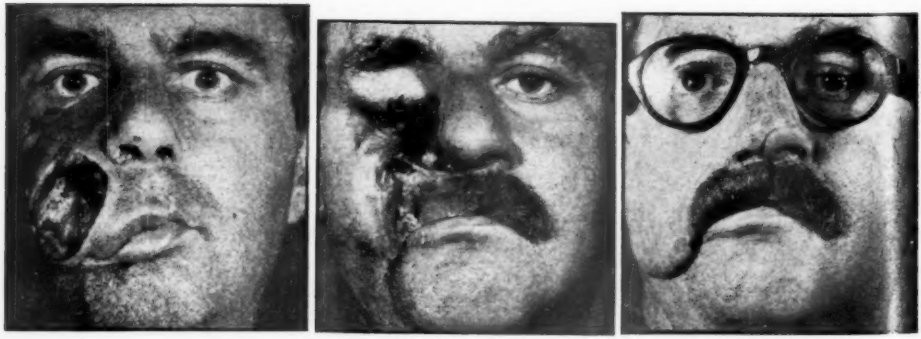
failed and this raises a doubt in my mind as to whether the ear, nose and throat surgeons are being radical enough in their surgery. Present methods of combined radiotherapy and surgery are undoubtedly a vast improvement on the old method of radical surgery alone. The curetting out of the tumour from within has proved its worth, but I believe that the time has come to revert more commonly to the earlier and more disfiguring operative approach, by cutting out the recurrent tumour from outside, dividing through uninvolved tissues and beyond its extensions. I speak as a general surgeon and my opinion is based on an experience of no more than fifteen radical excisions. However, most of these have been successful and every case was referred to me after radiotherapy and limited surgery had failed.

A B

FIG. 1.—Squamous cell carcinoma right antrum, total removal of right upper jaw and exenteration of orbit, with reflection of lip, and Crile's block dissection. A, Oral obturator in position. B, During reconstruction of face, to illustrate method of repair by means of the lined forehead pedicle flap.

The follow-up.—The initial full planned treatment must be supplemented by assiduous follow-up, so that recurrences can be spotted as soon as they develop.

The defect.—In planning the surgical attack on these recurrences, the first consideration is ablation of the disease, but a constant anxiety is the defect that inevitably results. The *internal defect* of palate and alveolus can, however, be made good with a dental prosthesis. These are now excellent, from the point of view of both function and appearance (Figs. 1 and 4). The *external defect* can be covered



A B C

FIG. 2.—A, Extensive squamous cell carcinoma of right antrum with necrotic oral fistula. B, Following excision of right upper jaw, face and lip and exenteration of orbit. C, The temporary prosthesis in position.

up by a prosthesis (Fig. 2c), which will enable the patient to face life again. But prostheses tend to leak saliva, beer and smoke and are not, therefore, as satisfactory to the patient as a new skin cheek. If the recurrence involves the floor of the orbit, then the eye of that side must almost always be sacrificed. It is a matter of weighing up the patient's life against one of his eyes and the patient himself usually has no hesitation in making the correct choice (Figs. 1 and 2).

In considering the defect one must remember that the very worst disfiguration of all occurs as a result of the continued growth of the tumour. Fig. 2A is a photograph of a man with persistent antral carcinoma fungating out on to his cheek, involving lip, nose and orbit and causing a stinking necrotic oral fistula. He is staring death in the face and a defect of almost any size (Fig. 2B) is an improvement on that circumstance, especially as there is a remote chance of a cure. The external prosthesis in his case (Fig. 2c) is only a temporary measure and we intend to replace his cheek in the near future.

The repair.—The patient illustrated in Fig. 2 will require a larger plastic operation than the lined forehead pedicle flap illustrated in Fig. 1B. This operation (Hunt, 1952) illustrates the principle that was often enunciated by the late Percival P. Cole, of the Royal Cancer Hospital, of repair by "local borrowing," and we have found it very successful in roofing over cheek and mouth defects in elderly people. The advantages of the method are that the patients are not immobilized in any way during the three stages of the operation and the whole process of repair is finished in a maximum of six weeks.

Plastic reconstruction of the face must not be begun until one may be reasonably sure that a further recurrence is not going to develop. However, it is not wise to defer the repair unnecessarily if the cavity can be examined by the removal of a palatal obturator.

Extirpation of the growth.—The operation of surgical extirpation must depend on the position and extent of the tumour rather than on its type. For example, radical upper jaw excisions have been done on 8 patients who were suffering from cancer of the upper jaw other than primarily of the antrum, which, as I have already mentioned, constitutes less than half the carcinomata of the upper jaw. In 3 the growth was a rodent ulcer extending into the bone, in 3 the primary tumour was in the alveolus, in one an extension from the buccal aspect of the cheek (Fig. 5) and in another recurrence of an adamantinoma of the lower jaw (which had extended up into the pterygoid laminae). One of the rodent ulcer patients (Fig. 3) is now over 80 years old and her defect is terrible. She has no

FIG. 3.—Long-standing terebrant rodent ulcer with destruction by growth, X-rays and surgery of face, upper jaw, nose and orbits.

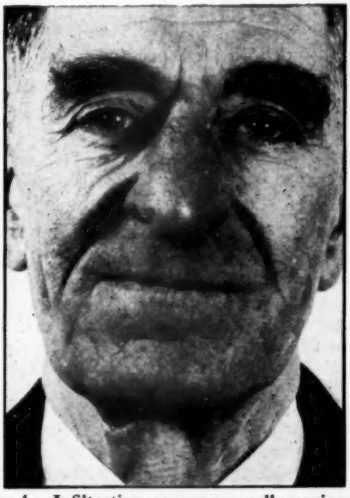


FIG. 4.—Infiltrating squamous cell carcinoma of upper alveolus and palate, internal prosthesis in position, seven years after double upper jaw excision through extensive Caldwell-Luc incision. (Right external carotid artery ligatured, left temporarily occluded.)

face, no upper jaws, no nose and no eyes, the destruction having occurred largely as a result of invasion by tumour but also as a result of radiotherapy and radical surgery. Yet she leads a fairly contented and moderately useful life. She covers her face with a mask which she makes herself out of gamgee and tapes, and she gets about as much as she wants to. She helps in the home, does the washing up, knits and so on. She is free from pain and there are no unpleasant discharges. Treatment in her case has been well worth while in spite of the appalling deformity.

In the case of alveolar carcinomata I have usually found it advisable to turn back the cheek in order to do a radical operation. Whenever necessary I cover the bare areas of the cavity with free-hand Thiersch graft mounted on a stent wax obturator.

Fig. 4 shows a man (a patient referred by Mr. John Cambrook) whose infiltrating squamous cell carcinoma had extended throughout the whole upper alveolus and palate. His operation was done more than seven years ago and he has led a normal life since. His appearance is also normal. The extirpation in this case was done through an extensive Caldwell-Luc incision running right round the upper gingivo-alveolar sulcus. The soft tissues of the face were stripped up off the bony framework, which was sectioned by chiselling backwards through both antra and the lower part of both nasal cavities, thereby removing the whole hard palate and both upper alveoli. Dressing consisted of no more than a temporary obturator of stent held in place by means of two thick pieces of stainless steel wire brought out through the mouth and attached to a plaster skull-cap. In this man's case the right external carotid artery was tied as a first stage to the operation, the left external carotid being temporarily occluded until hæmostasis had been secured, a procedure which undoubtedly is of great assistance in these gory operations.

Fig. 5 illustrates a patient who had had a carcinoma of the buccal aspect of the left cheek involving

FIG. 5.—Squamous cell carcinoma, recurring after radium therapy, of the left cheek and invading both jaws; to show the condition eighteen months after excision of left upper and lower jaws with Crile's block dissection of neck.

both upper and lower jaws, recurring after extensive radium therapy in Paris. The lymph glands of the neck were involved. Operation in this case entailed upper and lower jaw excision combined with Crile's block dissection of the neck. No skin was removed so external closure was easy and internal closure was effected by stitching the mucous membrane of the side of the tongue to the edge of the soft palate. The patient does not allow his oral disability and facial deformity to interfere with his life in any way whatsoever.

The decision as to whether or not a block dissection of the neck should be done rests entirely on an assessment of the state of the lymphatic glands by the operating surgeon.

The surgical extirpation, therefore, must be designed specifically and individually for each patient and no hard and fast rules can be laid down. For my part, I prefer a wide exposure and I always attempt to cut around rather than burning through tissue invaded by tumour.

In summary, therefore, I strongly advocate early and more radical surgical extirpation of all carcinoma remaining or recurring in the upper jaw, after the initial planned treatment has been completed, whether the tumour arises within the antrum or not.

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Mr. G. H. Bateman: In all but localized neoplasms of the lower part of the antrum I would recommend the approach described by Moure as lateral rhinotomy. This gives a better exposure than the sublabial approach and the ultimate disfigurement is very slight.

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Section of Laryngology

President—Professor V. F. LAMBERT, M.D., Ch.M., F.R.C.S.

[*November* 5, 1954]

The Rhinologist and the Orbit—Some Personal Recollections

PRESIDENT'S ADDRESS

By Professor V. F. LAMBERT, M.D., Ch.M., F.R.C.S.

It has been my good fortune to be associated with the Manchester Royal Eye Hospital as the Consulting Rhinologist for nearly twenty-five years, and it is the interest in the problems of diseases of the orbit which this appointment engendered that has prompted me to choose the subject for this Address. Rightly or wrongly, I have held the view that the orbit is one of the surgical territories which is of interest, not only to the ophthalmologist, but to the neuro-surgeons and ourselves. I share the view expressed by John Foster of Leeds (1948) that there is neither cash nor credit in the orbital tumours, and that the surgical treatment (and I quote him) is "deep, dark and bloody and not a gentleman's operation from the point of view of the Ophthalmologist". This applies to the rhinologist too. And yet I believe that our specialty has a place in the diagnosis and management of the surgical conditions of the orbital cavity.

A casual inspection of the orbital cavity will reveal that more than two-thirds of its bony walls are also the bony walls of the paranasal air sinuses. The roof of the orbit is, in a varying amount, the floor of the frontal sinus, its medial wall is made up of the paper plate of the ethmoid and at the posterior limit of this the sphenoidal sinus. Its floor is the upper wall of the superior maxilla which is, of course, the roof of the maxillary air sinus. From its very nature many of the diseases of the orbit arise from diseases of the air sinuses and diseases of the sinus walls.

The spread of inflammatory conditions from the paranasal sinuses to the orbit is facilitated by certain areas where the bone is excessively thin, amounting almost to a dehiscence, and it is by this loss of continuity of tissue that inflammatory processes may involve the orbit. In addition to this direct method, the spread of an inflammatory process may be by means of local blood vessels, as in the spread from the ethmoidal labyrinth by the anterior and posterior ethmoidal vessels.

William Benedict of Rochester (1949) divides the orbit into three divisions and three zones (Fig. 1). These three divisions are: (1) Subperiosteal; (2) the area between the periosteum and the cone of muscles; (3) the space embraced by the cone of muscles.

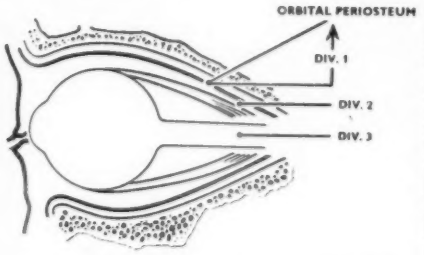

FIG. 1.—Division of orbital cavity—modified from Benedict (1949).

It is in the subperiosteal division that the lesions which interest the rhinologist present, because it is here that an infective process spreading from a neighbouring air sinus is likely to produce a periostitis, subperiosteal abscess or osteomyelitis, any of which may eventually give rise to an infection of the orbit. The bony tissue may also be subject to hyperostoses, malignant new growths, and the disorders of bone metabolism found in acromegaly, leontiasis ossea and the like. It is a fortunate state of affairs for us that any condition which we may be called upon to treat because it arises in bone will mostly be recognizable by careful X-ray examination.

There are three main signs which concern the rhinologist in intra-orbital diseases—firstly, displacement of the globe, secondly, alterations in the mobility of the globe, and thirdly the presence and nature of any recognizable swelling in the orbital cavity. I have omitted changes in the fundus of the eye and changes in the visual fields, as these are part of the ophthalmologist's own department.

Displacement of the globe of the eye, or "proptosis", implies the passive protrusion of the eye as a result of œdema, hæmorrhage or new growth in the orbital cavity. Exophthalmos is the term used when the eyeball is actively protruded, as in Graves' disease. The mechanism of this protrusion is not accurately understood, but in all cases of exophthalmos the forward displacement of the eye is accentuated as a result of spasm of the upper eyelid. I have never regarded the strict differentiation of this terminology as being very important, and I understand from my ophthalmological colleagues that they tend to use the terms "proptosis" and "exophthalmos" rather loosely, without implying any difference in the causative mechanism of the protruding globe. None the less, it is helpful in making a differential diagnosis, particularly when the condition is unilateral, to try to form some opinion as to whether protrusion is the result of a passive displacement from an orbital mass, or whether it results from thyrotoxicosis or other form of hormonic exophthalmos. If the upper eyelid cannot be everted or is only everted with difficulty, the proptosis is more likely to be due to thyro-

toxicosis or a hormonic exophthalmos, whereas if the lid is everted easily, then it is more likely that the eye displacement results from the presence of an intra-orbital mass. This test we know as Gifford's sign.

In the cases we have treated in our Department, the most common nasal condition to produce proptosis was mucocele of the frontal or ethmoidal air sinuses. From 1949 to 1953, 13 have been treated. Of these, 4 bore signs of acute infection and were producing acute inflammatory manifestations in the orbit itself. Their ages varied from 21 to 72. 7 of them were males and 6 females.

Of this group there is one case which I would like to mention.

The patient, a female, 49 years of age, was seen in the Neuro-Surgical Out-Patient Department by my colleague, Mr. Richard Johnson on December 14, 1953. She was complaining of undue prominence of the right eye which she said had been present for seventeen years. She was listed for operation at that time.

She had no diplopia, but had, from time to time, suffered from attacks of frontal headache and pain in the eye, associated with conjunctivitis. Investigations showed some field defect in the right eye. X-ray examination revealed marked destruction of the right orbital roof and a part of the greater wing of the sphenoid (Fig. 2). The appearances were consistent with a mucocele arising in the right frontal sinus, confirming the clinical diagnosis.

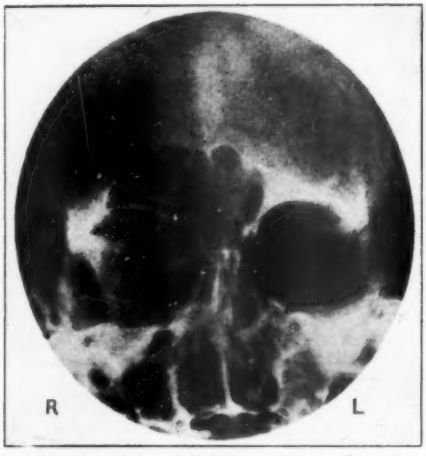

FIG. 2.—Mucocele destroying right orbital rim and part of greater wing of sphenoid.

In view of the extent of the mucocele involvement, my colleague, Mr. Richard Johnson, thought it unwise to rely on the orthodox route to the frontal sinus, offering as his opinion that the Dickson Wright (1948) approach to the orbit would give better access, and with this view I readily concurred. At this stage I shall describe this most useful method of exploring and decompressing the orbit.

It would appear from the author's remarks that it was developed because the older, classical operations of Kronlein and the trans-frontal method of Naffziger gave only a limited approach to the orbit and its contents. As a result of this limitation, an orbital tumour could be missed, and even if found, could only be removed with difficulty and sometimes at the price (and I have quoted the author) "of damage to nerves and muscles in the region with resulting disfigurement and disability".

The secret of an adequate approach is to remove a generous portion of the orbital rim as a free graft, and to replace it at the end of the operation. The particular quadrant to be removed is decided by the position of the lesion (usually a tumour) if it has been localized before operation. As a method of approach to the orbit for determining the site of tumours which it has been impossible to localize clinically before operation, it is necessary to remove the outer wall, or the outer wall and the roof, of the orbit, and through the openings thus made, the cavity can be explored with the finger (Figs. 3, 4 and 5). The author's method is as follows: An incision is planned 1 in. above the orbital margin and zygomatic arch reaching from the middle of the forehead to the auricle. The temporalis muscle is exposed after suitable retraction of the skin and the aponeurosis is incised 1/16 in. from the temporal ridge from the root of the zygoma upwards for 2 in. The muscle is retracted and the temporal fossa exposed. A spatula is then passed down the outer side of the orbit between the orbital contents and the bone, the periosteum of the orbital margin having been previously cleared. A drill hole is made through the outer wall of the orbit on to the spatula: this can be enlarged at will. The anterior cranial fossa may be opened if required, and by removal of the bone in the roof of the orbit and inwards

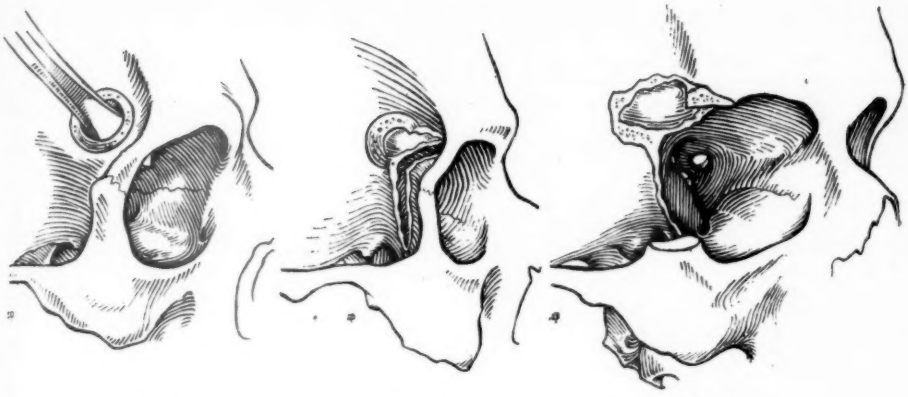

FIG. 3. FIG. 4. FIG. 5.

FIGS. 3, 4 and 5.—Steps of Dickson Wright operation illustrated on dry skull.

FIG. 6. FIG. 7.

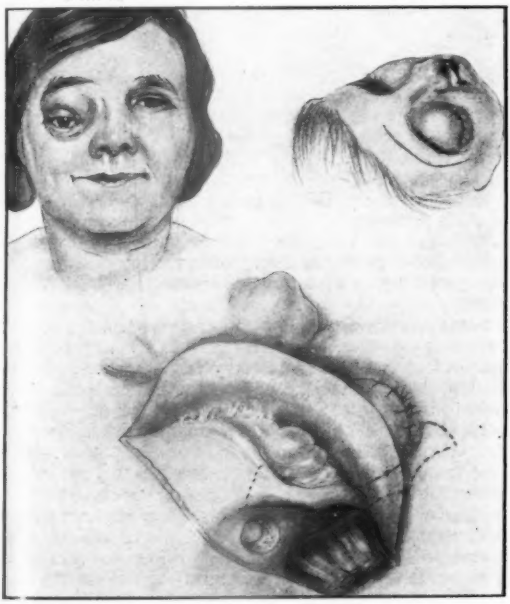

FIG. 8.

FIG. 6.—Pre-operative sketch showing severe displacement of eye.

FIG. 7.—Skin incision.

FIG. 8.—Skin flap turned down—mucocele presenting—temporalis muscle reflected—burr hole in temporal fossa. (Dotted lines represent segment of orbital rim removed.)

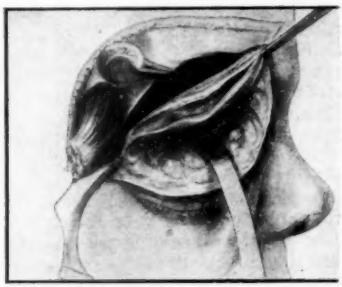

FIG. 9.—Segment of orbital rim freed but still attached to temporalis muscle. Lining of mucocele dissected.

FIG. 10.—Intranasal drainage completes the operation.

towards the sphenoidal ridge, the orbit and anterior cranial fossa thrown into one. When the exploration is being carried out for the recognition and removal of a tumour, its situation will dictate which part of the orbital rim is to be removed. This quadrant is removed by sawing, and is preserved for replacement at the end of the operation.

In our particular case (Figs. 6, 7 and 8) the lateral quadrant was removed and we allowed this to remain attached to the temporalis muscle. The exposure of the mucocele was excellent, and we

were able to dissect the lining from the ridge of the sphenoid and the upper eyelid without difficulty. A small portion of the mucocele was left as a cuff and was used to surround a drainage tube at the end of the operation, which was completed by a classical approach to the fronto-ethmoidal region through the inner angle of the orbit (Figs. 9 and 10).

It is extraordinary that the patient suffered relatively mild discomfort, despite the enormous size of the mucocele, and again despite its size, the co-ordination of the eye movements and other range of movements remained unimpaired. Even after the operation, there was only transient diplopia for a matter of a few days.

During this same period, we have been called upon to treat 8 cases of orbital cellulitis, and in all of them more than one air sinus was infected, the offending organisms appearing to be the staphylococcus and the streptococcus in about equal frequency. This bears out my personal experience of this problem over the last twenty-five years. As with so many of the acute infections in the field which demands our surgical interest, the whole picture has been changed since the introduction of the sulpha drugs and the antibiotics. I can recall in this pre-antibiotic era how the fashion seemed to change in regard to the surgical handling of orbital cellulitis in the absence of frank pus formation when the air sinuses had been pronounced clear of infection. We had waves of enthusiasm for incising the acutely inflamed orbital tissues to reduce pressure on the optic nerve and, we hopefully thought, to diminish the risk of central retinal thrombosis. Then we would have a spell when we would not incise the acutely inflamed tissue in the absence of pus formation. How in this phase of surgical fashion we loved to quote Wilfred Trotter—"When there is pus, let it out—but when there isn't pus, don't." That aphorism of his I read years ago, and also his remark that a scalpel never killed an organism. How often through the years have these admonitions restrained the aggressive scalpel? These problems do not appear to loom quite as large as they did then, because the antibiotics and the like are destroying the organisms and making one's surgical life much less exacting and much less harassing.

Pressure on the optic nerve is, of course, as pressure on any sensory nerve, a serious condition, and there appears to be some indefinable critical period and some indefinable critical amount of pressure which, if exceeded, produces irreparable damage to the optic nerve. It would appear that if this critical point is not passed it has amazing powers of recovery. In relation to this pressure effect on the optic nerve, Williamson-Noble in his paper to the Royal College of Surgeons on March 4, 1954, said that pressure on it from a subperiorbital hæmatoma is likely to produce permanent damage to the optic nerve unless relieved within twelve to twenty hours. If this be true, it is a very disturbing pronouncement, and calls for early relief of such pressure in subperiorbital hæmatoma from any cause. Not only should we take gross hæmorrhages into the orbital tissues more seriously, but I hope it will make us take a much more charitable view of some of the unfortunate happenings to the optic nerve which one has seen as a result of surgery to the accessory nasal sinuses, particularly those of us, who, so far, have not had such misfortune.

An interesting experience illustrating the powers of recovery of the optic nerve when the point of critical pressure on it has not been exceeded occurs to me. In January 1948 I did a Chiari transorbital operation for a chromophobe adenoma of the pituitary gland on a patient of Sir Geoffrey Jefferson's —a woman of 57. I chose to operate via the left orbit because the patient's vision on this side was reduced to the recognition of hand movements only. On the morning of the third day after her operation, she was able to count my fingers, and she said that for the first time with this eye she could see well enough to recognize my facial features. The improvement was continued, and eighteen months after the operation she wrote to tell me that the vision had been restored in this left eye. It was known that the vision had been quite useless for at least three months before the operation.

Over the four-year period which I chose for review for the purpose of this Address, there were no cases of cavernous sinus thrombosis. As a result of personal experience of septic conditions of the orbit, there are two views which I hold quite firmly. The first is that the greater proportion of orbital infections result from infection of the nasal air sinuses. Much suffering and anxiety can be saved for the patient if this fact is appreciated, and the causative sinus infection treated without delay. Secondly, I believe that in any acute stage of the sinus infection with orbital infections, whether it be a primary acute one or an acute flare-up of chronic sinus infection, the surgical treatment to the sinus or sinuses should be minimal. Simple drainage, or, as we call it in relation to the frontal sinus, decompression, is all that is required. If more ambitious surgery is undertaken at a later date, then it is far safer carried out when the flames of the acute process have subsided.

Fig. 11 illustrates a right orbital abscess secondary to a fronto-ethmoidal and maxillary sinus infection which has been treated by minimal drainage of the offending sinuses. There is a polythene tube in the right antrum: a small rubber drainage tube through the floor of the right frontal sinus and another rubber tube draining the orbital abscess independently. The appropriate antibiotic was used: the infection was the result of micro-aerophilic streptococcus.

The pseudo-orbital tumour or, as it is sometimes called, the non-specific granuloma is an interesting but puzzling group of swellings of the orbit which may present with a complete mimicry and masquerading of a new growth—irreducible proptosis, limitation of eye movements and a palpable tumour mass. Duke-Elder (1952) says that this inflammatory pseudo-tumour of the orbit is a clinical rather

than a pathological conception of a condition which has a very varied underlying ætiology. He believes that the group may embrace such widely separated conditions as sarcoidoses, the reticuloses, syphilis and tuberculosis and reaction around a foreign body. The three most recent that I have seen had a very widely different underlying pathology. In one the microscopical examination shows a number of foreign body giant cells, and the particular one shown in Fig. 12 appeared to be surrounding

FIG. 11.—Polythene tube in the right antrum. Small rubber drainage tube in soft tissues of orbit and in the right frontal sinus.

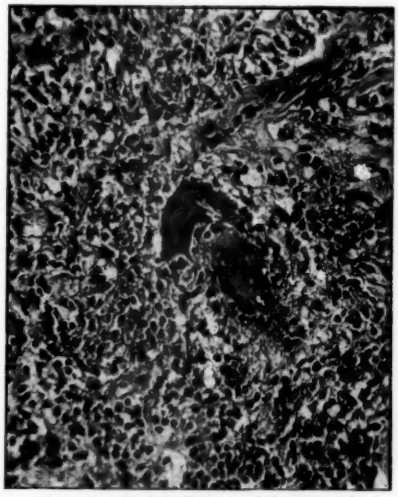

FIG. 12.—Refractile material present in foreign body giant cell. ×400.

some form of crystalline foreign body. There had been a previous history of trauma resulting from glass chippings going into the left eye ten years before the onset of subacute eye signs associated with forward displacement of the globe. The orbit was explored, but the nature of the lesion could not be determined. Following the exploration and parenteral penicillin, the condition appeared to settle, but flared up again twelve months afterwards, and this time biopsy of the tissue revealed a mass of chronic inflammatory granulomatous tissue with the refractile material present in the centre of one of the foreign body giant cells. To classify this refractile mass is not easy: I am informed by the pathologists that it could be a portion of suture material, perhaps even a piece of glass or some crystalline deposit resulting from dusting of the wound with a sulpha preparation. The occurrence of granulomata or pseudo-tumours around crystalline deposits of the sulpha preparations is pretty well recognized. I have been told that it was very common in Germany due to impure sulpha preparations, in the early days of their manufacture. We have had a number of cases of these granulomata in skin incisions in surgically treated breast cancer, and their presence has given rise to quite unnecessary alarm. It is interesting to speculate whether this second flare-up in the case which I have just described did result from the irritation of the sulpha—it would not, of course, account for the original trouble. The case I have quoted I saw with my colleague, Mr. Neville Young, who gave me permission to utilize the information for the purposes of this paper.

The other case is again associated with trauma, and the section of the tissue showed a picture highly reminiscent of the traumatic fat necrosis of the breast which clinically so closely simulates scirrhus carcinoma.

The third case I saw after a pseudo-tumour had been removed from the orbit. She presented at the Department with a chronic progressive subglottic œdema of such a severe degree that a tracheostomy had to be performed. A biopsy of this œdematous material revealed fragments of fibrous tissue, diffusely infiltrated with plasma cells and lymphocytes, the features of a non-specific type of inflammation. This report is very similar to the report of the biopsy of the eye tumour, except that the tissue of the eye tumour contained the lacrimal gland which also had features consistent with a chronic inflammatory condition of its structure.

These experiences have confirmed, if such be necessary, the view expressed by Duke-Elder (1952), namely, that the pathology of these pseudo-tumours varies, and labelling the condition is really a clinical label rather than a label of any definite pathological conception.

Of the osteomas which we have seen, only two have come to operation, one because of the double vision it was causing, and the other one because it was not only displacing the eye, but giving rise to

obstruction of the frontal ostium in an infected frontal sinus. The first one was operated on in conjunction with our neuro-surgical colleagues through a combined transfrontal approach and an approach through a modified lateral rhinotomy (Fig. 13). It was quite a considerable undertaking,

FIG. 13.—Osteoma of left fronto-ethmoidal region.

but the known result was satisfactory. The second case was much more straightforward, and the osteoma was removed through the standard inner canthus incision.

As I have read through the histories of the cases I have reviewed in the preparation of this paper, I have been impressed by the frequency with which trauma is mentioned by the patient as the precipitating cause of their orbital troubles. We are all familiar with the school of thought which regards trauma as the inherent factor in the ætiology of ethmoidal and frontal sinus mucoceles. Not until now has trauma impressed itself on my mind, this despite making allowance for a patient's natural desire and primitive instinctive blaming of all ills on some factor outside the body—and most of all, injury. Perhaps the most striking example in our orbital case is that of the unfortunate girl whose

FIG. 14.—Fullness of orbit—picture of patient when first seen.

FIG. 15.—Showing rapid growth of sarcoma.

picture is illustrated (Figs. 14 and 15). She came to the ward with this markedly proptosed eye with the history that she had been struck in the eye with a tennis ball fourteen days before. Beside the proptosis, the eyelids were red, giving the impression of a subacute inflammation, superimposed on what we thought likely to be an orbital hæmatoma. Subsequent events made only too clear that the real cause of the poor child's troubles was a rapidly growing sarcoma. Progress was checked for a time, by X-ray treatment, but she died from multiple secondary deposits.

Malignant tumours of the orbit are far from being a common condition, and in the records of the Christie Cancer Hospital and Holt Radium Institute I am only able to trace something under 70

cases of this condition since 1932 to the present time, and considering the general unsuitability of most cases of orbital tumour for surgical treatment, I think it is a fair assumption that this figure of just under 70 must represent a considerable share of orbital tumours occurring in the North-West of England.

I commenced my Address on perhaps rather a gloomy note in the early references to these tumours, and it is with a very brief mention of one case that I would like to end. This was a patient—a male aged 50—who was seen in January 1939 with a tumour of the upper jaw which was invading the orbit (Fig. 16). The tumour was a non-keratinizing squamous carcinoma, and, as will be seen from Fig.17,

FIG. 16.

FIG. 17.

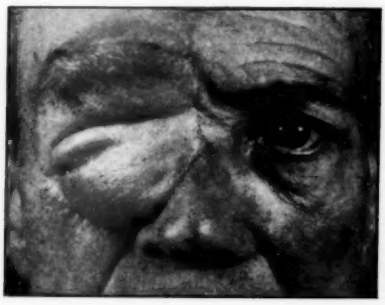

FIG. 18.

FIG. 16.—Tumour of upper jaw invading orbit.

FIG. 17.—Partial removal of upper jaw and exenteration of orbit, followed by treatment of cavity by radium.

FIG. 18.—Final stages of plastic repair.

the orbit was exenterated and a Moure's modified excision of the superior maxilla performed. A sorbo radium bomb was placed in the cavity—the patient is still alive to-day. Fig. 18 shows the repair of the defect: I could not match this result with any other of my own.

In the period of 1940–1944 my radiotherapy colleagues treated 21 cases with a 30% survival rate. Most of these tumours I fancy would be gliomas of the retina in children and scarcely fall within the province of the rhinologist, and, therefore, do not call for consideration in this paper.

Finally, I would like to stress again how seldom proptosis and diplopia occur as a presenting sign in post-nasal tumours. In the 132 cases which I surveyed in February of this year, only 7 of these first sought advice because of eye troubles.

One case of orbital tumour that came my way last year was spotted by a general practitioner who, when visiting a sick patient, noticed that another member of the family had a slightly proptosed eye which was otherwise painless and symptomless. It was ultimately proved that this was a secondary tumour resulting from a pelvic growth. We have had one or two other oddities and freaks of this type, but the story of these must wait for another day.

I would like to acknowledge the help I have received in the preparation of this paper from all my colleagues, both in my own Department and in the other Departments of the Hospital, and I shall not select anybody by name. My indebtedness is also due to the Departments of Medical Illustration of the Manchester Royal Infirmary and the Christie Hospital, to Miss D. Davison of the Department of Medical Art, and last, but by no means least, to my University Secretary, Mrs. Kathleen Barnes, for preparing the typescript and other duties connected with the compilation of the records.

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[*December* 3, 1954]

A discussion was held on **Malignant Granuloma and Scleroma.** Papers were read by Mr. GILBERT H. HOWELLS, Dr. I. FRIEDMANN, Mr. E. ZWIEFACH and Mr. E. J. GILROY GLASS. These papers will be published in the *Journal of Laryngology and Otology.*

The following took part in the discussion: Miss JOSEPHINE COLLIER, Mr. K. M. MAYALL, Dr. A. LASKIEWICZ, Mr. MAXWELL ELLIS, Mr. J. H. OTTY, Mr. S. W. ALLINSON, Mr. W. A. MILL and the PRESIDENT.

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Section of Obstetrics and Gynæcology

President—FREDERICK W. ROQUES, M.D., M.Chir., F.R.C.S.Eng., F.R.C.O.G.

[*November* 26, 1954]

DISCUSSION ON THE ÆTIOLOGY AND TREATMENT OF CORNUAL OCCLUSION OF THE TUBES

Mr. V. B. Green-Armytage: Intimate clinical study of secondary sterility, and of some cases of supposed primary infertility, often reveals a story of missed periods, and then of drugs, or aretus paste, or induced abortion, and/or curettage, followed, maybe, by the exhibition of antibiotics.

When patients with such histories are investigated by Rubin's test or hysterogram, it will be found that in the one case, gas-pressure-distension-pain is entirely suprapubic; whereas in the other, the X-ray film shows either rounded cornua *or that the oil* does not pass beyond the isthmus in over 90% of cases. Innocent spontaneous abortion is practically never followed by any form of tubal obstruction. Occasionally there may be a history of hysterotomy and ligation of the tubes, or of an ectopic, or of a classical Cæsarean section, or manual removal of the placenta.

In this paper I shall deal solely with post-conceptional infection of the secundines or inflammation of the endometrium and/or cervix which quite unwittingly and asymptomatically has given rise to a type of occlusion which very rarely indeed reaches beyond the isthmus.

This pathological type presents *at operation* a distal portion of the tube which is absolutely healthy and is therefore readily implantable. Such cases are usually seen in the young married or unmarried woman, but there is never any palpable abnormal pelvic pathology to help one in the diagnosis. Figs. 1, 2 and 3 illustrate the common postpartum types of stenosis met with in hospital and in private practice.

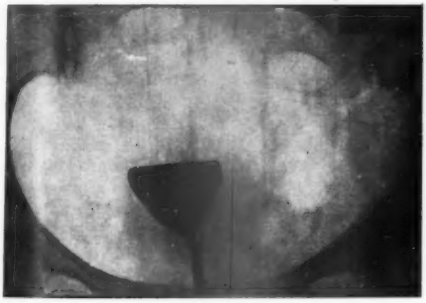

FIG. 1.

FIG. 1.—Criminal abortion before marriage showing rounded cornua. Distal portion absolutely healthy at operation of implantation.

FIG. 2.—Criminal abortion with isthmian occlusion both sides. Confirmed at operation. Distal portion absolutely normal.

FIG. 3.—Bilateral tubo-uterine implantation in the cadaver with subsequent hysterectomy showing P.T.F.E. in situ.

FIG. 2.

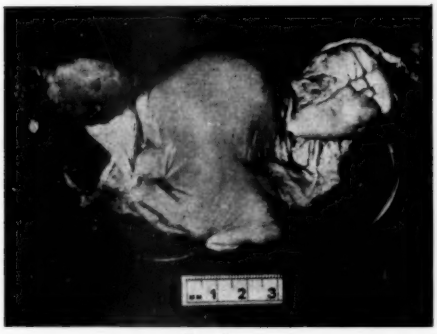

FIG. 3.

Until recently the ætiology and morbid anatomy of cornual tubal occlusion had received scant attention and the success rate was only 6%.

But to-day it is different for we know that if, *with such a case history*, there is no palpable pelvic pathology, no history of acute infection, and no clue of tuberculosis, together with negative gas and

oil tests, then at laparotomy the tubes are found to be stenosed at the cornu or for the length of the isthmus, but almost never as far as the ampulla.

The technique of tubal implantation is not difficult, nor does it take long, but it does need the utmost confidence of your patient, repeated expert CO_2 and Lipiodol investigations, together with meticulous instrumentation—all of which in time can be acquired.

For details of the operation, and the very necessary pre- and post-operative vitamin C and antibiotic treatment, *see* Green-Armytage, 1952.

There are a few new points which extended and recent experience has proven.

(1) The hysterogram must be done with Neo-Hydriol or Lipiodol (Lafay) and *not* with water soluble dyes such as Viskiosol, which give equivocal results and render deductions uncertain, though the new Salpix may be an exception. In addition a lateral picture should always be taken.

(2) Never use an air insufflating apparatus. The *danger* of air embolism at pressures over 150 mm. Hg is very, very real. To-day the Bonney Insufflator is a museum piece. Fifteen years ago I had a death on the table using it, and in a letter recently received from South Africa, 2 deaths in one week were recorded from air embolism using this method. Remember one MUST maintain, as Rubin states, a pressure of 200 mm.Hg of CO_2 for at least one minute, with or without the use of an antispasmodic such as octyl nitrite or pethedine, to form any real opinion. Such a thing as CO_2 embolism has never yet been recorded.

(3) Use polythene rods (P.T.F.E.) rather than polythene tubing, for there is a very definite risk of organisms and septic material passing by capillary attraction from the vagina up any tubing into the peritoneal cavity, thereby causing septic occlusion of the fimbrial ends, though the cornual anastomosis may remain perfect.

If for the lack of P.T.F.E. tubing must be used, then the inner end should be sealed by "flaming".

In the one case it is easily threaded through the tube; in the other it is best brought through on the end of a probe.

(4) Whichever material is used the intraperitoneal end must be secured to the infundibular ligament by catgut, lest by peristalsis it be extruded within a few days.

(5) The rodding (12 in. lengths) must not be more than 1·2 mm. in diameter and be antioxidant-free, to avoid injury or necrosis of the tubal mucous membrane. (Here I wish sincerely to thank Mr. Holt of the I.C.I. for his help in getting this material made for me by Messrs. British Insulated Callender's Cables, Ltd.)

(6) At the end of the operation always ventro-suspend the uterus. I prefer the plication method as the quickest.

(7) It is essential that the foot of the bed should be raised on 6–8 in. blocks for the first two or three post-operative days.

(8) After removing the P.T.F.E. rods vaginally (a painless procedure) at the end of six to seven weeks, request your patient to try and conceive during the next few ovulation periods.

(9) Finally I should say that according to Raoul Palmer in Paris, and Rock and Mulligan in America ampullary implantation is easier and even better than the isthmian. Decision can be made at the time of operation.

Results

Up to date I have done 20 consecutive tubo-uterine implantation operations for post-conceptional stenosis.

In only one case out of 20 at the time of laparotomy did the inflammatory process which had caused the block extend as far as the ampulla. In two-thirds it was not beyond the cornua or pars uterina.

5 out of these 20 have been operated upon within the last two months so they must be discounted. That leaves 15.

Of these 4 have gone to full term and been delivered by Cæsarean section. One by Professor J. McClure Browne; one by Mr. J. D. Murdoch and two by myself.

One is now 22 weeks pregnant. She is in the care of Mr. W. D. Frew in Edmonton, Canada.

One, a doctor's wife, has had 2 abortions at the third month.

This gives a conception rate of 6 out of 15=40% as against the old 6%. That it will be 60–70% soon, I feel sure.

I should like to mention one other case on whom the implant operation was done two months ago. She had had both tubes tied in the West Indies at the time of a Cæsarean section. That she will conceive, I have little doubt.

I have as yet had no case of ectopic pregnancy in this small series, though I have two such in another larger series of salpingostomies.

It should especially be recorded in the case sectioned by Professor J. McClure Browne, and in one of my own Cæsarean sections, that they both conceived within three months of the operation and that no polythene whatever was used.

Similarly in the one now 22 weeks pregnant in Canada, no polythene was used but she conceived two years after the operation.

Ipso facto a Cæsarean is not necessary though extraneous clinical conditions may, of course, indicate it. Raoul Palmer records 3 Cæsareans in 8 full-term patients.

9 patients have not conceived. For their follow-up I have to thank Mr. Alastair Gunn; Mr. W. McKim McCullagh; Miss J. Karniki; Miss Mary Barton and Mr. W. O'Sullivan.

In 4 cases there was recurrent stenosis at the cornua. In 2 of these this was, I think, due to the polythene being peristalted out of the uterus on the third or fourth day. In one a pelvic abscess developed, due, I think, to sepsis creeping up the tube.

2 out of 4 of these errors are now preventable.

In 2 cases both tubes are patent to gas and oil but they have not as yet conceived, one year later.

In 3 cases one tube only has remained open to gas and oil, the other having closed at the fimbria, I think due to sepsis spreading up the tubing, a thing now preventable by the use of solid rods.

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Miss M. Moore White: Bilateral tubal occlusion occurs in approximately 10% of sterile women. Tubal occlusion may occur at the uterine end of the tube, at the fimbrial extremity or along the course of the tube. The following figures for the site of tubal occlusion are quoted by Palmer (1950): Hamant 40% cornual, 60% fimbrial; Robins 18% cornual, 82% fimbrial; Kennedy 30% cornual, 70% fimbrial. Palmer analysing 250 cases gives the figure of 32% cornual, 52% fimbrial and 16% along the course of the tube. Under the title of cornual occlusion Palmer envisages occlusion at the utero-tubal junction or at the adjacent isthmian portion of the tube.

Cornual occlusion may be functional or organic. Repeated investigations may be necessary to distinguish functional from organic occlusion. Tubal spasm is a frequent finding when tubal insufflation is first performed, especially in nervous and tense patients. Sharman (1944), in a series of 60 cases subsequently examined radiologically after lipiodol injection, showed that insufflation had erroneously indicated blockage in 6 cases. Among his series of 116 patients who became pregnant, 29 had been diagnosed as having non-patent tubes as a result of a single insufflation. Spasm may be obviated by the use of sedatives and antispasmodics but may prove resistant to either or both given simultaneously. General anæsthesia has no greater effect than antispasmodics on tubal spasm.

Better results are obtained if an antispasmodic is taken for a day or so before the investigation. Spasm is more likely to occur at the time of ovulation; it is therefore wise to select a day forty-eight hours prior to the expected time. Knowledge of the operator, the absence of an audience, gentle handling, gradual introduction of the medium, which should be warmed if a fluid, lessens the likelihood of spasm. Spasm will often relax after a pressure of 200 mm.Hg has been maintained for two minutes.

ORGANIC TUBAL OCCLUSION

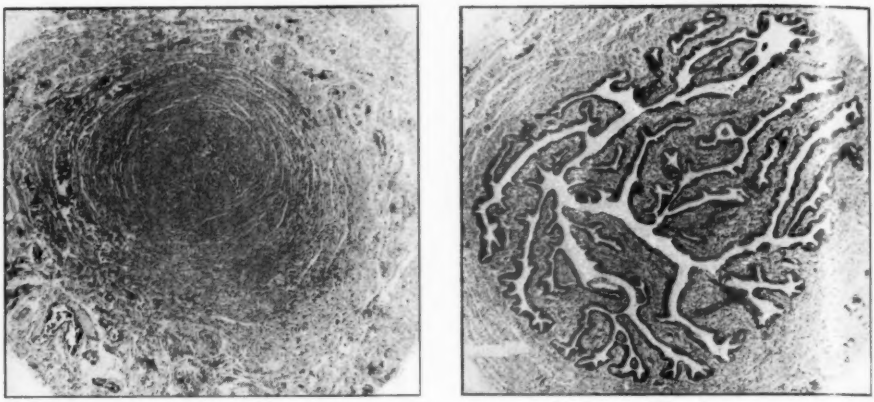
Organic occlusion (Fig. 1A, B) of the tube may result from: (1) Post-abortal and post-puerperal infections. (2) Trauma. (3) Gonorrhœa. (4) Tuberculosis. (5) Endometriosis. (6) ? Developmental anomalies.

Palmer (1950) states that 70% of cases of obliterations at the uterine end of the tube are accompanied by other tubal lesions. The largest group of cases of cornual occlusion are to be found in this group:

Post-puerperal and post-abortal infections.—Some of the infections in this group may be gonococcal in origin but the majority are streptococcal. In the post-abortal group a large percentage follow a criminal abortion. Some of the streptococcal cases may be associated with a history of pelvic pain, salpingitis or thrombophlebitis, but in others infection is confined to the uterus and tubes. In this group frequently other plastic operations such as salpingostomy or salpingolysis are necessary. It is not unusual to find one side more affected than the other. In a few cases there is no history of infection of any of the genital organs but the patient states that after the birth of the child she ran a low temperature for a few days, the cause was not known but uterine infection was suspected.

Trauma.—This may follow the introduction into the uterus of too hot a solution or too strong a chemical. It usually results from attempts by the patient herself or an accomplice to terminate a pregnancy. It can be assumed to have been the cause when the pathological section shows cicatrization and no inflammation in the tube beyond. It is possible that such a condition might follow a drastic curettage. It is possible, too, that faulty operative technique in performing a tubal suspension operation might produce a kink at the utero-tubal junction and obliterate the tube lumen.

Gonococcal.—When there is a preceding history of a gonococcal infection it is reasonable to assume that cornual occlusion results from this cause. Since the introduction of antibiotic therapy acute



A B

FIG. 1.—A, Fibrous occlusion at the cornu. B, Tube at site of implantation.

gonococcal infections may resolve but in the pre-antibiotic era and in some cases to-day they progress to a chronic infection. There is frequently extensive disorganization of the tubal mucosa and the likelihood of inflammatory nodules in the interstitial part of the tube and fimbrial occlusion. Because of the frequency of other tubal lesions the operative prognosis is difficult to assess.

Tuberculosis.—Tuberculosis of the tube appears, as a rule, to start in the outer part of the tube and only at a later stage to reach the cornual end. Haines (1952) is of the opinion that infection may extend from the endometrium to the tube. I cannot recall a single case of tuberculous endometritis in which there has not been prior impairment of tubal function demonstrated on the kymograph or salpingogram, and I am of the opinion that in by far the greater majority of cases the cornual end is not involved early. For this reason restoration of tubal patency is not likely to meet with success.

Endometriosis.—Endometriosis as a cause of tubal occlusion may be considered in the absence of any other possible cause. In thin women it may be possible to feel a nodular thickening at the cornu but, since nodules may occur in both tuberculous and gonococcal infections (although in the latter they are found more often in the isthmian portion), no definite diagnosis can be made. Endometriosis may be present elsewhere causing adhesions about the tubes and ovaries and lessening the otherwise good prognosis from operation.

Developmental.—Tubal occlusion may be present in a woman with uterine hypoplasia but since tuberculosis may occur in a hypoplastic tube and perhaps more readily so, a developmental origin for occlusion cannot definitely be accepted.

It will be seen from this series that the best results are likely to be achieved in the traumatic, the uncomplicated post-abortal and post-puerperal group and in tubal endometriosis.

OPERATIVE RESULTS

Rock, Mulligan and Easterday (1954), of 108 operations on one or both tubes using polythene tubing, reported 21 pregnancies in 18 patients, i.e. a pregnancy rate of 18%. Of these 4 aborted and 5 had ectopic pregnancies giving a total salvage rate of pregnancies of 11%.

Palmer and Boust (1950) reported 40 cases of tubal implantation with 13 pregnancies (32·5%), 3 ectopics (7·5%), 10 recurrences (25%) and 32·5% with satisfactory patency but no pregnancies. Palmer (1950) in a series of 10 cases in which he employed a fine ureteral sound to maintain patency reported carriage to term in 3 cases but in a later series 5 pregnancies were obtained in 10 cases with excellent permeability but no conceptions in 4 of the remaining cases. In this series of cases no accessory operation was necessary.

I have performed tubal implantation operations on 13 patients, 11 simple, 2 complicated (combined with salpingostomy) (Table I). Patency has remained at the uterine end in 18 of the 22 implanted tubes (Fig. 2) in one or both of the implanted tubes in 12 patients, despite the fact that no tubing has been left in situ. In 3 of the 11 simple cases there were fine adhesions about the ends of the tube or ovary. Two women have carried to term (18%), 3 have miscarried (27%), a 45% conception rate. In one of these and in 2 others subsequent fimbrial occlusion has resulted but in 2 chronic salpingitis was evident in the portion of the tube adjoining the site of section. 3 patients who have not yet conceived and 2 who have miscarried have good tubal peristalsis on insufflation and satisfactory salpingograms, that is 45% with good patency (Fig. 3). In the 2 cases complicated by salpingostomy cornual and fimbrial patency has remained in one, cornual only in the other. In both there was evidence of pelvic peritonitis and the other tube and ovary had been removed in one and involved in adhesions in the

TABLE I.—OPERATIVE RESULTS

Case No.	Tubes implanted	Patent at cornu	Patent at fimbria	Preg. or abort.	Long term result	Chronic salpingitis
1	2	2	2	i Tubal abortion ii A	Fimbrial closure	Yes
+2	2	1	1		Still patent	
3	2	2	2	P		?
+4	2	1	1		Fimbrial closure	Yes
+5	2	2	2		,,	
6	1	1	1	Early A	Still patent	
7	2	2	2	P		
+8	2	0			Occluded	Yes
9	2	2	2	A	Still patent	
+10	2	2	2		,,	
11	1	1	1		,,	Yes
Unilateral salpingostomy and implantation 12	1	1	1		,,	Yes
Unilateral salpingostomy and implantation +13	1	1	1		Occluded	Yes

\+ = Abortion produced by hot douche.
Case No. 3 = 8 attempts to terminate pregnancy.

other. There has been no complication in any case except for pulmonary collapse in one. She speedily recovered.

It is apparent from studying statistics that there is a percentage of approximately one-third of cases in which good tubal patency exists but pregnancy does not take place.

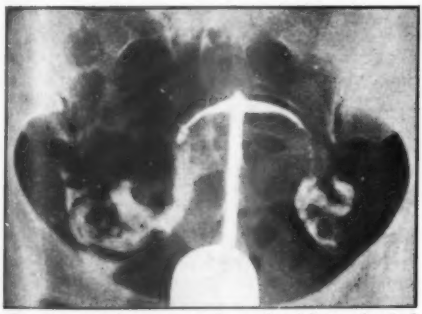


FIG. 2.—Salpingogram taken after bilateral tubal implantation.

If it were possible to overcome the raised abortion and ectopic rate and also bring about conception in the above-mentioned third of cases, tubal implantation could be considered a highly satisfactory operation.

A study of the physiology of the tube may help us to achieve this object. Reynolds (1949) states that the viability of the ova depends on the presence of a corpus luteum through the influence of which progesterone acts on the tubal epithelium. The ovum spends one day in the ampullary portion of the tube which is in a state of muscular activity and three days in the inner part of the tube which is by then quiescent, in its passage to the uterus. He states that it has been demonstrated experimentally that when the fertilized ova are retained in the ampullary portion of the tube they undergo degeneration within three days because they are denied access to that part of the tube in which the secretory epithelium is located.

If this concept holds when implantation is performed, and usually this is done about the junction of isthmian and ampullary portions, the ovum is deprived of its resting site in the inner part of the tube for three days and its life-maintaining nutriment. It may therefore fail to survive. It is difficult to conceive how an ectopic gestation results for, with a shorter length of tube and a wider lumen at the cornu, it would appear less likely. Admittedly the cilia have been removed with the inner part of the tube but some animals do not possess cilia and there is no indication that they are essential.

As regards the fertilized ovum that survives, it may enter the uterus at a three-day earlier stage of development than usual. It is just possible that the secretory cells of the uterine endometrium compensate for those of the tube but, on the other hand, they have not been under the influence of the corpus luteum for more than twenty-four hours and the endometrium is not adequately prepared, either as regards secretion or embedding, and the ova may degenerate or feebly embed, and a miscarriage result.

Since so much of our knowledge of tubal physiology is derived from different species of animals, opinions are bound to vary, and there are those who are not dogmatic regarding the time the ovum spends in the different parts of the tube, or the duration of its passage there, or the state of tubular muscular activity. Others do not think that the epithelial cells of the tube are concerned with the maintenance of the life of the ovum but think that the means of sustenance is contained within the ovum itself, since it can survive transportation to the anterior chamber of the eye or beneath the capsule of the kidney. W. J. Hamilton puts forward the suggestion that the ovum may pass too quickly into the uterus while still in an early stage of development and that, under the influence of the uterine

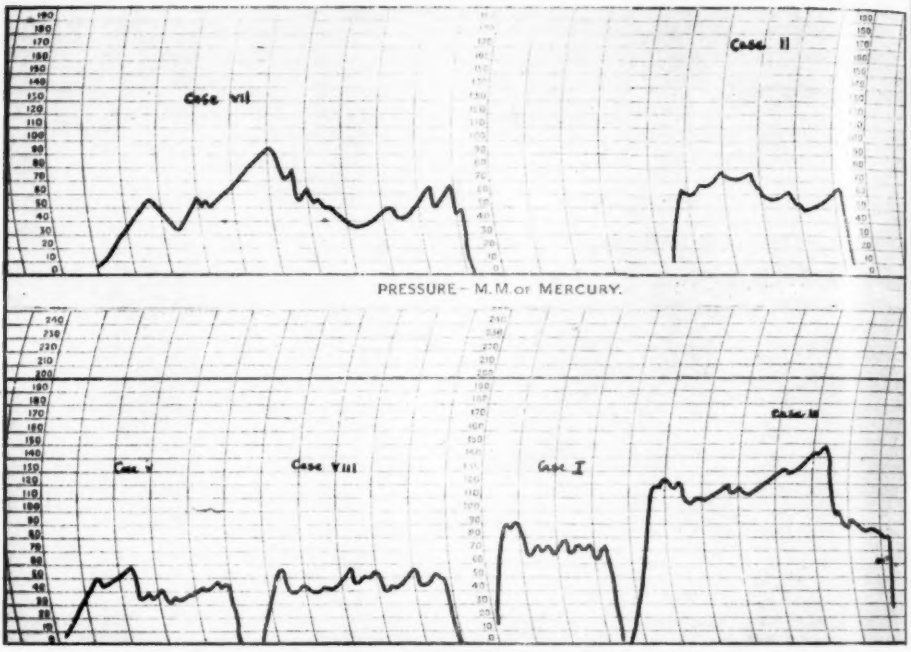


FIG. 3.—Illustrating typical kymographs after tubal implantations. [The numbers shown above do not correspond to the case numbers in Table I.]

secretion, it may lose the zona pellucida and perish since it is not ready for implantation until the blastocyst stage is reached. In this way many ova may be lost.

It has occurred to me that if œstrogens were given during the proliferative phase to further development of the endometrium and that if progesterone were given at the time of ovulation for three or four days and again about the twentieth day of the cycle, it might be possible not only to speed up the secretory phase of the endometrium but through the action of progesterone on tubal musculature to slow down the movements of the tube to delay entry into the uterus until a later stage of development and so to salvage some of the languishing ova.

It would be interesting if those of us performing tubal implantation operations could try this out.

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Dr. A. S. Bligh and Mr. Ewart O. Williams (Radcliffe Infirmary, Oxford): We attempt to evaluate some of the non-surgical causes of cornual occlusion and show how difficult it is to diagnose this condition and select those requiring surgery.

Stallworthy (1948) in his "Facts and Fantasy in the Study of Female Infertility" quoted figures from several authorities for tubal occlusion, varying from 26% to 50% and then reported his own figure of 12·8% and Jackson's of 10%. Stallworthy had reduced his apparent blockage figure of 21·6% by means of repeated salpingograms under fluoroscopic control and by the judicious administration of antispasmodics. We have continued this work.

Every case attending the fertility clinic with an apparent block shown by a Rubin's test, or failing to become pregnant within six months, is submitted to a salpingogram with fluoroscopic control. Our figures show that this is approximately 25% of all patients attending the fertility clinic.

Since February 1954 we have worked in close co-operation and during this time have performed 128 salpingograms together. Tables I and II show our results.

TABLE I

Total number of salpingograms	128
Total number demonstrating tubal occlusion.. ..	32 = 25%
Corrected rate for all cases seen at the fertility clinic	=6·25%

TABLE II

Number due to cornual occlusion at first salpingogram	17
Number later responding to antispasmodics, &c. ..	9
Number of "hard core" cases remaining	8 = 6·25%
Corrected rate of "hard core" cases	= 1·56%

It will be noted that the incidence of tubal blockage has fallen since 1932, when it was quoted as 26% to 50%, down to 6·25% and the incidence of "hard core" cases where cornual blockage can be blamed is only 1·56% of all cases attending the fertility clinic. We are still not convinced that this last figure cannot be further reduced.

[A series of salpingograms were then shown demonstrating how apparent cornual occlusion had been relieved by various methods including antispasmodics, heavy sedation, anæsthesia and changing the position of the uterus by means of the cannula.]

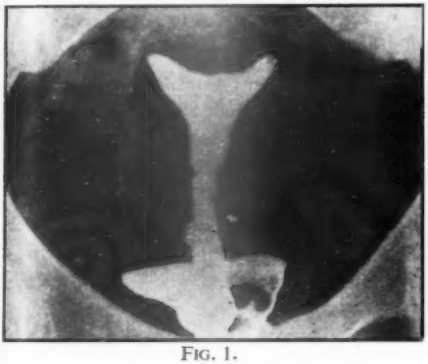

FIG. 1.

A series of X-rays were taken of a patient who had had a previous septic miscarriage and had been referred with a diagnosis of cornual occlusion. Fig. 1 shows our first salpingogram and appears to confirm the diagnosis. Later, by the exhibition of antispasmodics, we were able to obtain tubal filling, but no evidence of spill. She later had a Gilliam's suspension operation and at that time it was impossible to get air to pass through the cornua on retrograde insufflation; nevertheless, she was finally delivered of a live child without any surgical treatment of her fallopian tubes.

To summarize. Cornual occlusion is of very complex ætiology and we consider that it is usually a normal reaction on the part of the tubes to an abnormal stimulus. Whilst we keep an open mind on the possibility of a neuromuscular dysfunction at the utero-tubal junction, which may be a cause of infertility and be relieved by surgery, we hope to reduce our "hard core" cases even further.

One of the principal points in the technique of tubal implantation practised in the Area Department at Oxford is that the polythene catheters introduced into the fallopian tubes are tied together; this junction being inside the uterine cavity. This avoids any danger of the polythene slipping back into the peritoneal cavity, without long lengths hanging into the vagina with its danger of an ascending infection. The tubing is easily removed after dilating the cervix. We have cultured this tubing after removal and in all cases it has been sterile.

We would like to express our thanks to Dr. F. H. Kemp and Mr. J. A. Stallworthy for their help.

REFERENCE

STALLWORTHY, J. A. (1948) *J. Obstet. Gynæc., Brit. Emp.*, **55**, 180.

Mr. Wilfrid Mills (Birmingham): My interest in the treatment of cornual blockage by reimplantation of the fallopian tubes was aroused by the work of Mr. Green-Armytage and stimulated by the success of my first patient who was actually pregnant within two months of the operation. This was just two years ago and I have altogether performed the operation ten times. 4 of these patients had their operation within the last eight weeks and may thus be excluded from the results but of the other 6, 3 have succeeded in conceiving; between them there have already been four pregnancies which have produced two babies and two abortions.

In selecting cases I have preferred X-ray to insufflation, and I always use the watery solution of diodone which has caused very few reactions. I insist on two pictures at a month's interval showing the same absence of tubal shadow and I hesitate before operating when one tube is partially patent. These cases invariably seem to have had much more destructive salpingitis and there is less chance of finding a healthy ampullary portion in the tube with cornual obstruction when its fellow is blocked in the isthmus or ampulla. I have been surprised to find more than once at operation that a tube which gave negative tests to insufflation and two negative X-rays was indeed patent but severely stenosed. I believe that the operation may be indicated in such cases of acquired stenosis and also in the rare case of congenital stenosis due to hypoplasia.

Regarding technique I try to avoid all unnecessary manœuvres. I insufflate with Bonney's instrument to demonstrate the block at operation. I core out the cornu with the Silcock punch and splint

the tube with polythene tubing during its implantation, the tubing being then removed. I try to operate soon after the menstrual period and I formerly performed hystero-salpingography on the tenth post-operative day. I have now given this up as it seems unnecessary therapeutically as well as diagnostically.

In conclusion I believe that the operation of reimplantation of the tubes is indicated in most cases of cornual blockage. The most successful patients will be those who have already proved their fertility by having a previous pregnancy and in whom the ampullary ends of the tubes retain their normal function.

Mr. John Stallworthy (Oxford) said that he wished to congratulate Mr. Green-Armytage on his remarkable success following tubal implantation. Having said this, however, he felt it only right to make it clear that there were views held by both Miss Moore White and Mr. Green-Armytage with which he had never been able to agree.

One of the most important concerned the diagnosis of cornual occlusion. The main problem was not the technique of operation but the correct selection of the case for which operation was justly indicated. All who had performed the operation with success, as assured by subsequent pregnancy, knew that there was no technical difficulty and no great finesse required. The diagnosis of organic cornual occlusion was, however, a most difficult one.

In 1947, after several years of intensive study of this problem, he had published the Oxford results based on a study of over 1,000 consecutive cases. At a time when the world literature suggested that from 25–50% of all women complaining of infertility had tubal occlusion, the Oxford work indicated that the correct rate was more in the neighbourhood of 10%. The reason for the difference had been the general failure to recognize the importance of functional occlusion as opposed to organic lesions. This could be well illustrated with reference to Mr. Green-Armytage's Fig. 1. The rounded cornua to which he drew attention, and which were, he claimed, indicative of all cornual occlusions, were nothing of the sort.

This view put forward by Mr. Green-Armytage was the recognized teaching in textbooks, but it was incorrect.

They had seen the slides demonstrated by Dr. Bligh, and had seen pictures similar to the ones shown by Mr. Green-Armytage, in which pregnancy had proven tubal patency without any surgical interference being necessary.

The speaker emphasized the great difficulty in diagnosis, and the ease with which patients could be selected for operation, when in fact no organic blockage existed.

He stated that after many years of careful study of this particular problem, he for one was unable to diagnose with assurance a cornual occlusion on either kymographic or radiological evidence. He felt that the major point to stress was the low incidence of cornual occlusion as demonstrated by Dr. Bligh and the danger of operating unnecessarily.

Dr. Raymond G. Cross (Infertility Department, Rotunda Hospital, Dublin) suggested a modification in the technique of the use of polythene tubing which he, himself, had to use owing to technical difficulties during one case. The modification was that he threaded the polythene tubing through one tube, across the fundus of the uterus and out through the other tube. He then took the two ends of the polythene and incorporated them loosely in the abdominal wound, crushing the ends and tying them in a knot outside the abdomen. He had encountered no difficulties and felt that it was a cleaner method in that it avoided capillary attraction infection.

He hoped soon to have lined up a sufficient number of cases of genital tuberculosis already treated by PAS and streptomycin from which he could select suitable cases for tubular implantation with polythene tubing protected by an umbrella of PAS and streptomycin and isoniazid.

Mr. Green-Armytage, in reply said that no one, and least of all himself, who had been doing hysterosalpingograms every week for the last thirty years, would dream of disputing what Mr. Stallworthy and Mr. Williams had said on the matter of simple spasm of the tubes simulating organic blockage. As he stated at the beginning, he was dealing with the ætiology of organic occlusion of the tubes secondary to induced, criminal or incomplete abortion, together with postpartum infections which had prevented further conception.

Repeated investigation of such cases by oil and gas tests had indubitably demonstrated cornual and isthmian obstruction only. Moreover, subsequent laparotomy had shown that such cases with such histories presented themselves with distal portions of the tubes absolutely healthy and therefore readily capable of implantation.

As regards the well-illustrated method spoken of by Mr. Mills, and written up by himself (1937, *Brit. med. J.*, ii, 6) he would say that this technique was now *vieux jeu*, for there was not only the risk of the tubes becoming cyanosed and later compressed by the uterine muscle, but he and others had recorded ruptures of the fundus before or during labour. Mr. Mills' figures gave a 30% success for this operation, but the one he was advocating would, he hoped, in the near future exceed the 40% success they had now attained.

Proceedings of the Royal Society of Medicine Vol. 48 95

Section of Orthopædics

President—R. W. BUTLER, M.D., M.Chir., F.R.C.S.

[*November* 2, 1954]

Condylar Fractures of the Knee-joint

By T. J. FAIRBANK, F.R.C.S.

THIS is a plea for the treatment of condylar fractures of the tibia, and to a large extent of the femur also, by continuous traction and immediate movement without any further immobilization whatever. It is also a plea for the avoidance of open operation. While a few have followed methods similar to those to be described, the majority of writers on this subject lay great stress on the importance of accurate reduction of the displaced fragments and prolonged immobilization both to maintain reduction and to allow torn ligaments to repair. Watson-Jones has recommended a period of ten weeks in plaster. Where manual reduction or the use of some form of clamp still leaves an unattractive radiological appearance, open reduction is often advised, particularly on the other side of the Atlantic. Bolts, lag screws, blade plates, bone grafts and other devices have all been recommended in an attempt to maintain what is only rarely perfect reduction, and to support the pulverized articular surface.

Tibial condylar fractures are most common after middle life—in this series 30% were over 60 years of age. It is difficult from the published work to estimate the success of the treatment, but it is hard to believe that there were not many stiff knees, and certainly quite a number came to arthrodesis.

In the method to which I was first introduced by our President, the routine of treatment is as follows. After aspiration of the hæmarthrosis if necessary, a Steinmann pin is inserted through the tibia below the fracture level; there is no advantage in transfixing the fragments, and there are a number of possible disadvantages. The fracture is reduced manually as far as possible. It is obvious that a fully congruous joint surface is ideal, but perfection is very rarely attained, and in my opinion this makes but little difference since a severely depressed and irregular surface seems to carry but little worse prognosis than a mild displacement. The leg is supported by counter-balanced slings under calf and thigh, and active movements are started at once. Traction of 5–7 lb. is maintained for about a month—or even eight weeks, depending on the patient's progress. The patient is then allowed up on crutches, but no weight-bearing is permitted for three months from the injury.

One occasionally sees a patient with little swelling and good movements who can be treated on crutches from the start.

In this series, apart from one immediate fusion, done some years ago for reasons we would no longer accept, only one arthrodesis has been required out of some 50 tibial condylar fractures. We can reckon on recovery of almost full knee movement in weeks, whereas by other methods one reckons in months. Some of our cases were shown at the B.O.A. meeting at Cambridge three years ago, and for the purpose of this paper an analysis and follow-up were made on 13 femoral condylar fractures and 52 tibial condylar fractures. Fractures of the patella and of the tibial spines have been deliberately excluded.

Condylar fractures of the lower end of the femur can in general be divided into three groups:

(1) The complete "mush", where a poor result will follow any treatment.

(2) The Y-shaped fracture, where the force is apparently transmitted straight down the shaft of the femur; the shaft with its stronger cortex survives and is driven like a wedge between the two femoral condyles, which are split apart with varying amounts of comminution and rotated so that their articular surfaces tend to face towards each other. These are often severe fractures, and some of them are better treated on some form of Thomas's splint hinged at the knee for the first few weeks.

(3) Isolated fracture of one condyle, usually the lateral, which is forced upwards and is often rotated, so that the upper spike points somewhat backwards. If manipulation under traction fails to restore reasonable position, this is, in my opinion, almost the only fracture in the group which should be subjected to open operation and screw fixation.

There are also three types of tibial condylar fractures.

(1) Inverted T-shaped fractures, with varying amounts of comminution and displacement of both tibial condyles, due, one may assume, largely to longitudinal force. The lateral condyle is almost always the more severely damaged, the articular surface of the medial condyle remaining intact and the fracture line passing upwards *lateral* to the tibial spines.

(2) Fractures involving one condyle, almost always the lateral, from a combination of longitudinal force and valgus or varus strain. This is the so-called bumper fracture. There is often some lateral subluxation of the knee, and one may suppose that the degree of comminution depends on whether the condyle is smitten broadly by the main articular surface of the opposing femoral condyle, or

whether lateral subluxation occurs first, so that the margin of the femur is driven down into the midst of the tibial condyle. When this happens a large fragment may be split off the tibia. In both cases there is damage to the internal lateral ligament, and often to the cruciate ligaments also. I believe that the differentiation of these two types is quite unimportant, and is mainly of radiological interest.

(3) Fractures of quite small fragments from the margin of the tibial condyle, the mechanics of which are obscure.

Results

When one has seen the results of other methods, one cannot fail to be impressed by the speed and excellence of function regained by patients treated by traction and immediate movements. The great majority returned to their old employment with minimal or no symptoms from their knees. The longest follow-up was for eleven years, and other writers have already remarked on the surprisingly long time that these severely damaged joints last without any symptoms of degenerative arthritis.

Only three of the tibial condylar fractures had less than 90 degrees of flexion after three months. The majority had an almost full range of movement long before this period. Almost all the severe fractures lacked the last few degrees of extension, but this did not seem to trouble them in any way. I think this is due to the posterior part of the condyle bearing the brunt of the impact and remaining more depressed than the anterior margin. Not one was seen with symptoms attributable to a damaged meniscus. Only four showed slight laxity of the internal lateral ligament on examination, and none had symptoms due directly to this ligamentous insufficiency. Where there has been severe depression of the lateral tibial condyle it was usual to find some residual valgus deformity, but this did not seem to vitiate the final result.

In the severely comminuted fractures of this type perfect reduction is unattainable. I think this would be admitted by all who have had the salutary and chastening experience of operating on them. The depressed area is composed of a mush of fragments of bone, cartilage and meniscus, and the cavity filled with blood clot. Left undisturbed this turns to granulation and then fibrous tissue, and the early movements smooth off the new articular surface. When this new tissue is firm enough, the added stimulus of weight-bearing probably produces metaplasia into fibrocartilage. I do not think this new tissue necessarily ossifies to any great extent; at least one is often struck by the persistence radiologically of an apparently large hollow in the tibial condyle in a knee which has complete lateral stability.

If this is indeed the best articular surface that we can hope for, then the less we interfere with the natural process of repair the better. The only essentials are to guard against weight-bearing and lateral strains, and to encourage movement from the start. Continuous traction and immediate exercises provide for these requirements.

To me the really puzzling factor in the success of this treatment lies in the fate of the torn ligaments. In the isolated tear of the internal lateral ligament, whether operative repair is done or not, almost all would agree that a long spell of immobilization is essential to ensure later stability. One can only suppose that in these fractures the ligaments are less severely damaged. Clinical proof by forced movements during the primary examination is, however, contra-indicated by its risk of increasing the bony deformity. In any case, the fact remains that under this regime repair is adequate.

This method is supremely simple for both patient and surgeon, and I submit that it produces better and quicker results than any other.

A Classification of Fractures of the Pelvis

By M. Pickering Pick, M.B., B.S., F.R.C.S.

Fractures of the pelvis may be divided into two main groups, namely: isolated fractures of the pelvic bones, and fractures of the pelvic ring. This paper is concerned with the classification of the fractures of the pelvic ring.

If the ring is broken at one point, it remains stable. If, however, it is breached at two points, either by a double fracture, a fracture dislocation or a double dislocation, it becomes potentially unstable and may be widely disrupted.

Stable Fracture of the Pelvic Ring

This is the commonest fracture of the pelvis, and is caused by a fall on the side. On the X-ray (Fig. 1), the fracture runs through the ischial and pubic rami, at the weakest point of the ring. There is never much displacement. Reduction is unnecessary, and moreover, because the ring is stable, fixation is unnecessary; treatment of this injury therefore presents no difficulty, all that need be done is to teach the patient, whilst he is in bed, to regain control of the leg on the injured side. He is instructed to lift the leg with the knee straight, and in this position to rotate it in and out at the hip. When he can do this, and not until he can do this, he may get up and be taught, first to stand and then to walk. Weight-bearing may be allowed from the start, as further displacement does not occur. Complications involving intra-pelvic structures do not occur with this type of fracture.

Unstable Disruptions of the Pelvis

Disruptions of the pelvis are a different matter, because the ring may be unstable, displacement may be grotesque, and intra-pelvic injury, particularly to bladder and urethra, is relatively common. The disruptions may be subdivided into three types, depending on the force which produced them. These are the compression fracture, the hinge, and the vertical fracture. Although the vast majority of the disruptions may be placed quite clearly into one of these three groups, one occasionally comes across an instance in which the force has obviously been a mixed one, and, of these, the commonest is the compression hinge fracture.

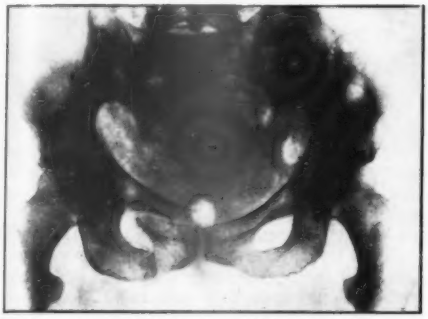

Fig. 1.—Stable fracture of the pelvic ring.

Fig. 2.—Compression fracture.

The Compression Fracture

This is caused by a crushing force. The patient has commonly either been buried or run over. On the X-ray (Fig. 2), all four rami are fractured. Displacement is not usually gross. Treatment does not vary much from that described for the previous fracture, because the ring, although unstable to a compression force, is stable to weight-bearing. The patient may take rather longer to regain control of the legs, but he may be allowed to take weight as soon as he is able, because further displacement with weight-bearing does not occur.

The important point about this fracture is that it is liable to be complicated by injury to the urethra or bladder. It has been estimated that, of those who survive the initial trauma, 10% have either a ruptured bladder or a ruptured urethra. In this small series of 30 cases of disruptions of all types, there were 4 ruptures of the urethra, all of which occurred with this type of injury. There were no cases of injury to the urethra with any other type of disruption.

The Hinge Fracture

In this, the force acts from before backwards, and impinges upon the pelvis in the region of the anterior superior spine. A common way for this to happen is when the victim falls from a moving vehicle, even a bicycle, landing half on his face and half on his side in the road, and being thrown over. Radiography shows that half the pelvis is hinged open. Posteriorly, the sacro-iliac joint is dislocated; in front, there is a separation through the symphysis pubis, or there is a fracture close alongside it (Fig. 3).

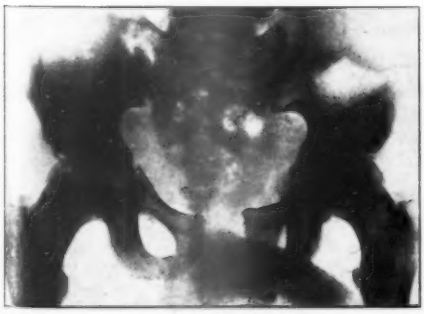

Fig. 3.—Hinge fracture.

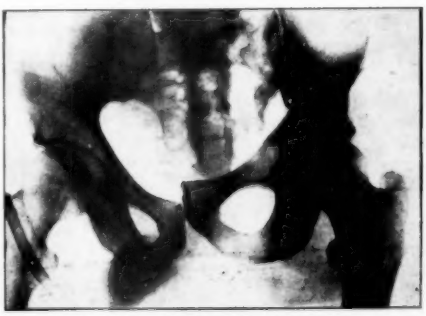

Fig. 4.—Rotation hinge fracture.

There is a variant of this injury called "the rotation hinge" (Fig. 4), in which half the pelvis is rotated backwards. One of the ways in which this may occur is when a rider is rolled on by his horse. The treatment of both these injuries is to reduce the dislocation by manipulation under anæsthesia. Once reduced, the ring is relatively stable, and the reduction may be held by a binder or a wide webbing belt. No rigid fixation is required since it is unlikely that the pelvis will again be subjected to hinge force. Thereafter, treatment follows closely that already described. The patient can usually start to walk on the sound leg and a pair of crutches by the end of the third week, and should have discarded his crutches at the end of six weeks. It is unusual for this type of disruption to be complicated by injury to the bladder or the urethra, but it is of interest to note that in 2 cases in this series there was hæmaturia. In both cases it occurred on the day after the injury, the original urinary specimens being clear, and was presumably due to primary damage to the kidney.

The Vertical Fracture

The force travels from below upwards, and is caused either by a fall from a height, or a blow from behind, such as might be sustained from the wing of a motor-car or the buffer of a locomotive. On the X-ray (Fig. 5), there is a fracture of the ischial and pubic rami on one side, and either an upward dislocation of the sacro-iliac joint, or a vertical fracture through the ilium or sacrum immediately adjacent to it. Half the pelvis is displaced upwards. In treatment, the upward displacement can usually be reduced by skeletal traction applied to the leg, which should be maintained for six weeks. At the end of this time, the patient may be allowed to get up, but because this disruption is unstable to weight-bearing, crutches should be used for a further six weeks. Again, injury to bladder and urethra is uncommon with this fracture, but there is a complication which seems to be peculiar to it. This is sciatic nerve palsy. Lam (1936) reviewed the literature and found that nearly 1% of fractures of the pelvis were complicated by peripheral nerve injury. The sciatic, the gluteals or the lateral cutaneous nerve of the thigh, may be damaged. Presumably the nerves are stretched as they run over the rim of the pelvis during the upward displacement. In this series, there were 2 cases, one complete, and one partial, of sciatic nerve palsy; both recovered spontaneoulsy.

Fig. 5.—Vertical fracture.

Summary

Fractures of the pelvic ring are subdivided into the stable and unstable. The stable fracture is easy to treat and is uncomplicated. Of the disruptions, a compression injury is stable to weight-bearing, but is commonly complicated by injury to the bladder and the urethra. The hinge fracture, once reduced, is stable, and complications are unusual. The vertical fracture is wholly unstable to weight-bearing, which must be prevented for twelve weeks. This injury is liable to complication by peripheral nerve damage.

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Some Unusual Cases of Tendo-vaginitis Stenosans

By W. G. Doig, M.B., B.S., F.R.C.S.

Tendo-vaginitis stenosans was described first by De Quervain in 1895. The most usual sites of its occurrence are two; the first at the styloid process of the radius where the tendons of the abductor pollicis longus and extensor pollicis brevis with their sheaths are affected, and the second is the typical "trigger finger" found in both adults and infants. It can also occur elsewhere, as the following case histories will show.

Case I.—Miss M. A., now aged 60.

She suffered an inversion injury of her left ankle in June 1949, and since August of that year noticed a "cracking" sensation on the inner side of the foot just below the medial malleolus. This was only present on active movements and expecially on plantar flexion of the big toe. In August 1950 the flexor hallucis longus tendon was explored and, at the operation, the narrowing of the tendon where it passed under flexor retinaculum was easy to see (Fig. 1). Her symptoms were entirely relieved by the operation.

In October 1950 she noticed a similar "cracking" sensation on the inner side of the other, i.e. the right,

ankle, and again on active movements of the big toe. At operation (November 1950) the constriction was again easily seen (Fig. 2). Her symptoms were completely relived by operation.

In September 1954 she was operated on for typical "trigger fingers" of the middle fingers of both hands with complete relief.

FIG. 1.

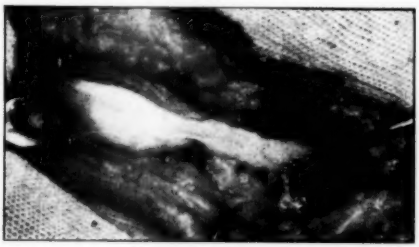

FIG. 2.

Case II.—Miss G. N., aged 17. Ballet student.

Since the age of 6 she has been ballet dancing, but seriously only in the past year. Four months ago, for no reason, her left ankle began to hurt. She then went on holiday for nine weeks, at which time she had no symptoms as she was not dancing, but on her return the pain came back after only one hour's practice. This was especially noticed on landing with the foot everted, and she also noticed a "clicking" on plantar-flexion of the ankle. No physical signs could be obtained on passive movements but, when she actively inverted and plantar-flexed the foot, a definite click could be felt just below the medial malleolus. This was not apparent on movement of the big toe only.

At present, no operation has been done, but I feel certain that, when it is, the tendon of the tibialis posterior will be found to be constricted, and its sheath probably thickened.

The literature reveals only one other case affecting the flexor hallucis longus tendon, although there have been quite a number of cases written about the tibialis posterior tendon.

Case III.—Mrs. G. S., aged 43. Housewife.

She was first seen in August 1954 with a history of seven months' pain in her left wrist on flexing her middle and ring fingers. After this was accomplished with difficulty, the fingers would straighten with a painful snap felt in front of the wrist. She could not remember why it started.

It was causing her enough disability to warrant an operation, and about September 1954, the carpal tunnel was explored. When the flexor retinaculum was incised, the flexor tendons bulged through and the synovial sheaths were very thickened (Fig. 3).

The synovial sheaths were excised and she has remained quite symptom-free since the operation with a full, active, painless range of movement.

FIG. 3.

Case IV.—Mr. R. M., aged 29. Stonemason.

This man complained of intermittent pain in the right wrist for three and a half years, so severe that he had to give up his work and became a cable-joiner's mate.

There was an almost complete absence of physical signs and it was even suggested that his trouble was functional but fortunately he was seen in one of his more severe attacks, and there was definite tenderness on active movement of fingers and a suggestion of swelling in front of the wrist. A similar operation to the last one was performed, again with complete relief.

SUMMARY

Four cases illustrating some of the unusual types of tendo-vaginitis stenosans are described. They show the value of the history and of the patients' own active movements as aids to diagnosis and they point out the danger of labelling as functional that which cannot be at once diagnosed.

I should like to thank the Consultants of the Orthopædic Department of the London Hospital for permission to use their cases.

Treatment of Traumatic Madelung's Deformity by Shortening the Ulna

By F. C. DWYER, M.Ch.Orth., F.R.C.S.

ALTHOUGH varying degrees of traumatic separation of the lower radial epiphysis are extremely common, one seldom encounters partial or complete epiphyseal arrest. Those cases in which arrest of growth occurs are of interest not only because of their rarity but because of the deformities, the disabilities and the problems in treatment they present.

The arrest of growth may be of even character (Fig. 1) but as a rule it is irregular, giving rise to abnormal tilting of varying degree as well as shortening of the lower end of the radius. Most commonly the arrest is on the volar and ulnar aspect causing obliquity as seen in Figs. 3 and 4. Occasionally backward tilting (Fig. 2) or even more rarely, obliquity towards the radial side is seen (Stephens and Wood, 1954). Because of the shortening of the radius the ulna projects distally giving rise to a prominence on the dorsal aspect of the carpus (Figs, 2, 3 and 4). If there is marked backward tilting due to arrest on the dorsal aspect of the radius, the ulna may project on the volar side of the carpus (Anton, Reitz and Speigel, 1938) but this is rare. In addition to shortening of the radius one sees widening of the space between the lower ends of the two bones (Figs. 1, 2, 3 and 4).

FIG. 1A.

FIG. 1B (Reversed print).

FIG. 1A.—Male aged 15 two years after complete separation of lower radial epiphysis. Note uniform arrest of growth, shortening of radius and widening of interosseous space.

FIG. 1B.—Two years after shortening of the ulna. In spite of the head never reaching the ulnar notch the patient had a strong wrist with no symptoms when in the army three years after operation.

FIG. 2A.—Male aged 16. Left wrist two years after an injury which caused very slight separation of the lower radial epiphysis. Note shortening, obliquity towards ulnar side and slight backward tilting of lower end of radius.

FIG. 2B.—Aged 20, four years after operation when patient had full movement and function, with no pain or weakness. Note the way in which the two bones have come together.

Of the 6 patients suffering from traumatic arrest of growth at the lower end of the radius, there was wide separation of the epiphysis associated with a fracture of the ulna in one instance and this was followed by uniform arrest of growth (Fig. 1). In the remaining 5, the initial displacement was very slight and considerable deformity resulted (Figs. 2, 3, 4 and 5). This has been noted by other authors (McFarland, 1931, and others) and suggests that in each instance there must have been a severe degree of direct compression when the injury occurred.

FIG. 3A.—Male aged 15. Right wrist four years after minimal slip of lower radial epiphysis. There is marked volar and ulnar tilting with overgrowth of the ulna and wide separation between the lower ends of the bones. This patient presented the most severe deformity and the pictures illustrate the degree of growth disturbance which can follow direct compression.

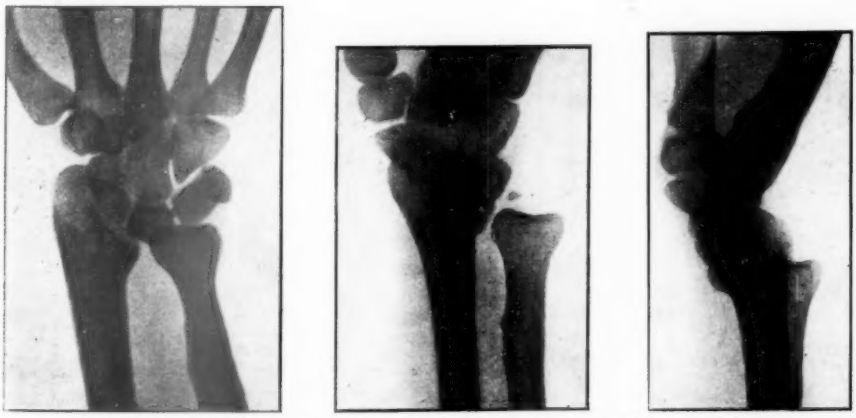

FIG. 3B.—Six years after shortening of the ulna. Strength was normal, rotations were full and the patient was working as a builder's labourer. In spite of the residual tilting an osteotomy of the radius was never necessary.

The type of growth irregularity which occurs leads to stretching of the attachments to the triangular fibro-cartilaginous disc and serious interference with the mechanics of the inferior radio-ulnar joint. The progress of the deformity depends upon the degree of arrest which is usually not absolutely complete. Troublesome symptoms as a general rule begin to make their appearance two or three years after the original injury, and are as follows:

(i) Gradually increasing deformity with abnormal prominence of the lower end of the ulna. (ii) Increasing weakness of grip. (iii) Pain with use and tenderness of pressure. (iv) Clicking, particularly on supination. (v) An abnormal degree of antero-posterior mobility between the radius and ulna combined with limitation of supination. (vi) Appreciable broadening of the wrist.

FIG. 4A.—Female aged 7. She had fallen and hurt her left wrist three years before but the injury was not regarded as severe. At this stage the ulna was shortened so as to bring its head proximal to the lower end of the radius and, as was expected, the deformity gradually recurred.

FIG. 4B.—The same patient four years later and just after the ulna had been shortened for the second time. Growth is not complete and further operative treatment will be necessary.

FIG. 5.

FIG. 6.

FIG. 5.—The wrist of a female aged 52 two years after excision of the lower end of the ulna. Her wrist had troubled her ever since an injury at the age of 15. When 50 years of age another fall caused aggravation of symptoms. Note the oblique lower end of radius, the medial slip of the carpus and complete lack of support on the ulnar side. Her wrist was weaker and more painful than before operation.

FIG. 6.—The left wrist of a man aged 47 ten months after shortening of the ulna and an osteotomy of the lower end of the radius. He returned to work on the docks.

In 6 of the patients the deformity was treated by shortening the ulna. Burrows suggested shortening of the ulna in 1937 and H. Milch described his operation of cuff resection in 1941 and again in 1942. This procedure was decided on in preference to excising the lower end of the ulna as described by Darrach (1936) because it was felt that without the support of the ulna there might be a tendency for

the carpus to shift towards the ulnar side. That this decision was justified was shown, not only by the results, but by the disastrous effect which followed excision of the lower end of the ulna in the seventh patient (Fig. 5). In that case the carpus did, in fact, shift towards the ulnar side, leaving the patient with a more painful and much weaker wrist than before. There can be little doubt that had the ulna been shortened in this case the final result would have been much better.

In adults, where fractures of the lower end of the radius have united with appreciable shortening and distal projection of the head of the ulna, similar symptoms may result. In such cases it is felt that shortening of the ulna is likely to give a better result than excising its lower end (Fig. 6).

The operation of shortening the ulna is quite straightforward and is performed through an incision on the dorso-medial aspect of the lower end of the forearm. A longitudinal cut about 3 in. in length is made in the long axis of the ulna with a mechanical saw. The bone is then divided at either end and an appropriate section removed from each tongue. As a rule there is no difficulty in pulling the distal fragment proximally for the inch or so which is usually required. Unless growth is already complete the head of the ulna should be brought to a point proximal to the notch on the radius to allow for subsequent growth. If much shortening is required it is quite safe to divide any restraining bands one finds in the soft tissues, including the ulnar collateral ligament. When full correction has been obtained the stepped fragments are held in position by means of two screws. After a few weeks in plaster full movements and good function are regained in a surprisingly short time.

Results

This operation was performed in 6 patients, 5 of whom were suffering from traumatic Madelung's deformity, whilst in the sixth the shortening of the radius was due to a fracture dislocation in adult life. 5 were operated on over three years ago and in 3 of these, five or more years have elapsed since the operation. The adult suffering from a fracture dislocation of the lower end of the radius was operated on only eleven months ago (Fig. 6). All have good strong and stable wrists which they are able to use strenuously. All have full movement and cosmetically they have been improved. One patient (Fig. 4) is only 11 now and has been operated on twice, the first time being four years ago. Her wrist is perfectly satisfactory but further operative treatment will be necessary. The lower end of the ulna was excised in one case (Fig. 5) producing a very poor result due, it would appear, to loss of support on the ulnar side.

Summary and Conclusions

In children arrest of epiphyseal growth at the lower end of the radius results in deformity, interference with the mechanics of the inferior radio-ulnar joint and considerable disability. In adults, fractures causing appreciable shortening of the radius also gives rise to similar symptoms. Treatment depends upon restoring the normal relationship between the lower ends of the two bones and, in particular, getting rid of the abnormal pressure caused by the distal projection of the lower end of the ulna. This can be most satisfactorily and safely achieved by shortening the ulna in the manner described. It may be necessary in certain cases to correct the abnormal tilt at the lower end of the radius but excision of the lower end of the ulna is not only unnecessary but may well cause increased disability and weakness. The correct operation in these cases is to shorten the ulna. Besides providing support for the carpus, the head of the ulna with the attached triangular disc is left in a reasonably correct relationship to the lower end of the radius.

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Spastic Valgus of the Foot

By R. Merryweather, F.R.C.S.

A review is presented of 60 patients with spastic valgus of the foot. There is clearly no one cause of spastic valgus and its ætiology is not clear, but certain ætiological factors are discussed, in particular the role of the talo-navicular joint in the causation of spastic valgus. However, an impression will be given of some possible causes, and a classification provided, whereby a prognosis might be made at the beginning of treatment.

In the present series examples have been found of different recognized types, but 31 of the cases (51·7%) had no developmental anomaly of the tarsal bones. With one exception the review has been confined to cases of spastic valgus occurring in adolescence.

Of the 60 patients in our series, 45 were boys and 19 of them were heavily built. 41 of the cases were unilateral and 19 bilateral.

The degree of spasm varied. In the most severe it involved the extensor digitorum as well as the peronei. It has seemed feasible to differentiate between spasm and the adaptive shortening described by Harris and Beath (1948). Many of the cases with tarsal anomalies started with spasm and finished with adaptive shortening.

Full radiographic examination was carried out on all the cases.

This included antero-posterior, lateral and oblique views of the tarsus; posterior projection of the subastragaloid joint, described by Harris; and an antero-posterior of the ankle.

Table I is an analysis of the 60 cases into their various types.

TABLE I.—SPASTIC PES VALGUS

60 *cases*

Tarsal anomalies 40%		No tarsal anomalies 51·7%	Other causes 8·3%
Calcaneo-navicular bar	Medial talo-calcaneal fusion		
9	15	31	5

(1) *The calcaneo-navicular bar.*—There were 9 patients with calcaneo-navicular bar; 6 were bilateral and 3 unilateral. The antero-posterior view of the tarsus is sometimes more valuable than the oblique for settling the doubtful cases with a long anterior process of os calcis. Those with no bar show a definite space between os calcis and navicular in this view. Of these cases one was treated by bilateral excision of the bars. He eventually lost his pain, but never regained any subastragaloid movement. 3 were treated by triple arthrodesis and did well; 3 conservatively treated did equally well, but none regained normal subastragaloid movement.

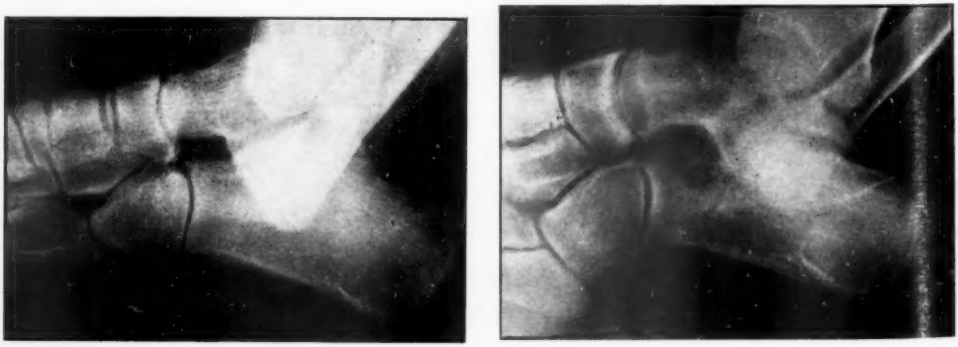
(2) *The medial talo-calcaneal bridge.*—There were 15 examples of this anomaly, of which 9 were quite definite and 6 not conclusive radiologically, though clinically very suggestive. Clinically a foot which will not invert under anæsthesia probably has a medial bridge, provided there is no calcaneo-navicular bar or osteoarthritis.

The special view recommended by Harris may be open to misinterpretation. However, it will give a definite answer in many cases.

None of these patients has been subjected to arthrodesis because each already has a fixed sub-astragaloid joint.

(3) *Cases with no anomaly.*—All of these 31 patients had badly pronated feet. With treatment 16 either lost all spasm and regained full subastragaloid movement, or spasm was only provoked by over-use; 10 are too recent to assess.

Of the 11 who failed to regain any subastragaloid movement, all have osteoarthritic changes in the talo-navicular joint. In some this was present when they were first seen. Others developed the complication while under treatment, sometimes rapidly (Fig. 1).



A B

FIG. 1.—To show the development of osteoarthritic changes in the talo-navicular joint. Eighteen months elapse between films A and B.

It happens that in those who did well treatment was started early (average age 13½ years), while those who developed osteoarthritis were seen later (average age 15 years).

(4) *The special causes:* (*a*) Tuberculous ankle. (*b*) Infective lesion of tarsus. (*c*) Osteochondritis of neck of talus. (*d*) Osteochondritis dissecans of ankle. (*e*) Fracture of navicular.

(*a*) A young girl who reported with two months' history of a painful ankle. She had protective spasm of peronei and dorsiflexors and increased warmth, with rarefaction of the bones radiologically. Biopsy of synovial membrane proved tuberculous infection of primarily synovial type.

(*b*) Child of 10. This patient was treated several years ago and made a full recovery. Her notes and radiographs indicated an infective lesion in the tarsus with considerable rarefaction.

(*c*) Woman of 44. History of only six weeks' pain. Was found to have spastic valgus without tarsal anomaly or X-ray changes. Was treated conservatively for two years. During this time she developed a lesion on the under side of the neck of the talus with the eventual formation of a small loose body (Fig. 2). Arthrodesis was performed and the affected area of bone was sent to the pathologist, who confirmed the diagnosis of osteochondritis.

FIG. 2.

FIG. 3A.

FIG. 3B.

FIG. 2.—A rarefied area on the under side of the neck of the talus, with a small loose body which was not present on previous films.

FIG. 3.—Osteochondritis dissecans of the upper medial border of the talus (A). Healing of the lesion is shown one year later (B).

(*d*) Boy of 12. Two years' history of pain; a cavus foot with no external tibial torsion; marked peroneal spasm. Radiographs showed osteochrondritis dissecans of the upper medial border of the talus.

The protective nature of the peroneal spasm can easily be appreciated. One year later the lesion had healed (Fig. 3).

(*e*) Girl of 17. In October 1953 sustained a fracture of the navicular; treated in plaster for one month and then on exercises without weight-bearing. Commenced weight-bearing after three months. In August 1954 she developed a marked spastic valgus of the foot and radiographs showed osteoarthritic changes in the talo-navicular joint.

TREATMENT

Most of the patients in this series were treated by periods of immobilization in plaster, generally in inversion, and usually preceded by manipulation of the foot.

A primary examination of the foot under anæsthesia is an aid to diagnosis since if the subastragaloid joint is fully mobile there can be no tarsal anomaly. It is doubtful if any further advantage is gained. The foot should be held as nearly as possible in the physiological position. The minimum period of plaster treatment should be six weeks and in cases with severe spasm it is an advantage to keep the patient off weight for the first few weeks. Thereafter, an outside iron and inside T-strap is a good appliance, often combined with a Thomas's heel and a valgus pad in the shoe. This is used as long as pain or spasm persists and is then gradually discarded.

This regime is suited equally to those with and those without tarsal anomalies, but, of course, the criteria of cure are different. Those with tarsal anomalies are protected until spasm has diminished and pain has gone—the same applies to those without anomalies, but with osteoarthritic changes. In neither of these groups must we expect normal subastragaloid movement to return.

Those with medial talo-calcaneal fusion were, by the nature of the anomaly, unable to regain any subastragaloid movement; some of those with calcaneo-navicular bars did regain a little rotatory movement of the coalesced navicular and os calcis around the head of the talus.

In cases without anomalies and no osteoarthritic changes, if the joints of the foot tend to relax, protection is worth continuing until there is no further tendency to go into spasm.

Arthrodesis.—Triple arthrodesis was performed in 8 cases of the 60. As with arthrodesis in other situations, the main indication was persistent pain, unrelieved by conservative treatment. 4 of these patients had calcaneo-navicular bars, 4 had osteoarthritis but no anomaly. The pain was presumably arthritic in all of them. There will probably always be this hard core of cases requiring triple arthrodesis.

Excision of calcaneo-navicular bars.—This operation was performed in only one patient (bilaterally). Pain was relieved, but subastragaloid movements have never returned.

Excision of ligaments in sinus tarsi.—This has been performed on 3 feet, 2 in the same patient. Neither case had tarsal anomalies. One appears to have done well and now only gets spasm after a heavy day's work. This was the unilateral case. In the other case, the excision on one side was followed some time later by triple arthrodesis. Both feet have remained rigid and there is now nothing to choose between them.

Scheme of treatment recommended.—(i) Plaster in physiological position (after examination under anæsthetic, if this has been considered necessary for diagnosis).

(ii) Off weight three weeks in severe cases.

(iii) Plaster retained at least six weeks.

(iv) Outside iron and inside T-strap until: (*a*) Foot relaxes in those with no anomaly or osteoarthritis. (*b*) Pain goes and spasm lessens in those with anomaly or osteoarthritis.

(v) Triple arthrodesis in a few cases with persistent pain.

In considering the *ætiology* it has been most striking to notice in this series that osteoarthritic changes, when present, occur primarily in, and are always most marked in, the talo-navicular joint. It may, perhaps, be assumed that the joint which suffers most is the responsible joint. Certainly it is reasonable to suppose that in the presence of an inter-tarsal fusion, such as has been described, the talo-navicular joint is subjected to abnormal stress. In those without anomaly the condition occurred always in a badly pronated foot in which the navicular was markedly deviated laterally on the head of the talus. Most observers agree that an irritative lesion in the tarsus must be the responsible factor, but it does not seem likely that the ligaments in the sinus tarsi can be blamed, as these could hardly be responsible in those patients with medial fusion where there is no movement between os calcis and talus.

The theory that the talo-navicular joint is the responsible one has been borne out by the special case in which osteoarthritic changes, resulting from a fracture of the navicular, precipitated a typical spastic valgus.

In spastic valgus of the foot we are dealing with a disordered state of muscle function which is common to all types and which may be provoked by a variety of different lesions. The treatment in the majority is directed towards the relief of this muscular dysfunction and the possible prevention of its sequels. Rest, relief of pain, protection and re-education all have their part to play.

Classification and Prognosis

Type I.—Spastic valgus without tarsal anomaly or osteoarthritic change. Attending at an early age with short history, one may reasonably expect a cure.

Type II.—Spastic valgus without tarsal anomaly, but with, or developing, osteoarthritic changes in the talo-navicular joint. These cases will not regain subastragaloid movement, but may well become painless on conservative treatment. Arthrodesis will be necessary occasionally.

Type III.—Spastic valgus with tarsal anomaly (calcaneo-navicular bar or medial fusion). Normal subastragaloid movement cannot return. Therefore, protection can often be dispensed with much earlier than in Types I and II, provided pain has been relieved.

Type IV.—The special causes must be borne in mind. In particular, osteochondritis dissecans in the ankle or subastragaloid joint may be missed unless a thorough X-ray examination is carried out.

Acknowledgments

My thanks are due to Mr. Norman Capener, F.R.C.S., for permission to publish details of these patients, all of whom have been treated at the Princess Elizabeth Orthopædic Hospital, Exeter.

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Section of Ophthalmology

President—HUMPHREY NEAME, F.R.C.S.

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Leprous Affection of the Eyes

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My contribution to the consideration of this matter is a brief one. I wish to leave to others all description of details and to confine myself to trying to outline a general background into which the detailed account of leprous eye involvement may fit.

Many ancient accounts of leprosy mention the chronic inflammation of the eye, often leading to blindness, which is characteristic of the severer forms of the disease.

Perhaps the first real attempt in modern times at a sound scientific description of leprosy was made by the Norwegian workers Daniellsen and Boëck over a century ago. Their work was illustrated by a magnificent series of coloured plates. Only a few days ago my old mentor and colleague, Dr. Ernest Muir, while on a visit to Norway, was presented with a set of these coloured plates, several of them illustrating the eye lesions of leprosy which he has passed on to me.

SOME GENERAL CONSIDERATIONS

The old conception of leprosy as essentially a skin disease is, or should be, dead; leprosy is to be regarded as a systemic infection.

The disease shows itself in two main forms, now termed "lepromatous" and "tuberculoid", although there are cases which do not fit well into either of these two main groups.

In the lepromatous form of leprosy the infection is widespread in skin, mucous membrane, nerves, bone marrow, some internal organs, and also in the eyes, and there is little or no attempt of the tissues to react or to localize the infection.

In the tuberculoid form of the disease the infection is much more restricted, often being confined to certain areas of skin and to local lymph nodes and certain nerves, although there have been recent reports of some lesions in the internal organs; bacilli in the lesions are few, and tissue reaction to them, with resulting localization, is a marked feature.

Now with these widely differing forms of leprosy, widely differing forms of eye involvement may be seen, and without going into any detail I wish to mention them.

LEPROMATOUS INFILTRATION OF THE EYE

This is seen as part of the generalized systemic infection of lepromatous leprosy, and it constitutes the most serious of the leprous eye infections. I will mention only a few points.

First its frequency. It used to be considered that lepromatous infiltration of the eye was characteristic only of severe generalized lepromatous leprosy. During recent decades the better methods of examination available, particularly the slip lamp, have shown that even in the relatively mild lepromatous cases a degree of lepromatous infiltration of the eye is very common, although it frequently produces no marked symptom.

Secondly, its severity. Those who have seen leprosy in various countries have, I am sure, been struck by the marked regional variations in the severity of leprous eye lesions. On the plains of India and in West Africa, where most of my work has been, severe leprous affections of the eye are seen, but much less commonly than in some other countries which I have visited. For example, I once visited a leprosarium in Kashmir where over 50% of the patients were partly or completely blind. I have noted that in Chinese patients, in Anglo-Indian patients, in South American patients and in European patients, severe leprous eye affections seem to be relatively common. Similar local variation is seen in some of the other serious manifestations of leprosy, for example, involvement of the larynx. There does seem to be a definite racial factor operating in these matters.

Thirdly, I would mention the effect of chemotherapy. First I would mention its effect on leprosy in general. In my experience before the introduction of sulphone therapy, the prognosis of lepromatous leprosy was often bad; treatment could only delay the downward progress, and death was the usual outcome, frequently accompanied by partial or complete blindness. Our present treatment of leprosy has many shortcomings, but the hopelessness of the past should not be forgotten. But I would also stress the value of chemotherapy, particularly in the prevention of serious eye lesions. I quote from my personal experience. In Uzuakoli, in Eastern Nigeria, where I worked from 1947 to 1954, there were in 1947 about 20 patients with severe eye involvement, partly or completely blind. Chemotherapy of leprosy then introduced could control the leprosy, but could not restore

the sight. The value of chemotherapy was seen between 1947 and 1954 in the marked fall in the incidence and in the severity of lepromatous eye lesions. This was very striking. During this time chemotherapy undoubtedly prevented serious eye complications in a considerable number of patients.

I will not discuss treatment in detail. Sulphone treatment (diaminodiphenylsulphone given orally), if necessary in small doses, and cortisone, given either as eye drops or by subconjunctival injection in the acute phases, were the main measures. In some cases, thiosemicarbazone was used instead of sulphone.

Tuberculoid Eye Involvement

By this I mean the direct involvement of the eye in the inflammatory process of tuberculoid leprosy. Tuberculoid leprosy is localized, and usually the eyes escape, but there are cases in which the skin of the face is involved, or the part of the face round the eyes, and thus the eyes may be involved directly with tuberculoid inflammation of the conjunctiva and cornea. This in itself is not very serious; it usually subsides in a few weeks, with little permanent damage. It does become serious, however, when, as is not uncommon, there is an ascending tuberculoid involvement of the V and VII cranial nerves, with subsequent palsy. This is discussed below.

Paralytic Lesions of the Eye

These may arise in two ways. The first way has already been mentioned, the ascending neuritis from tuberculoid lesions of the face, but it can occur in lepromatous leprosy also. In lepromatous leprosy the nerves are involved, but are often little damaged because of the lack of tissue reaction. As the disease dies down, however, either spontaneously or under chemotherapy, the fibrosis of the nerves which accompanies healing may lead to destruction of nerve fibres and paralytic changes in various parts of the body, including the eye.

I will not describe the condition in detail; the characteristic findings are inability to close the eye, ectropion, lagophthalmos, loss of corneal reflex, and, in consequence of these changes, the complete destruction of the protective mechanism of the eye.

Conclusion

I have tried to give some general background to the picture of leprosy of the eye. In conclusion I would state my opinion that practically all serious eye involvement in leprosy is preventable, by early diagnosis, and thorough general treatment of leprosy. In very few cases does the eye become seriously involved in the earlier stages of the disease. If all cases could be promptly diagnosed and thoroughly treated, serious leprous eye lesions would also all be prevented. That is my experience in many hundrds of cases during the last seven years. Unfortunately, I believe that many of the cases seen in this country are relatively advanced when they come here and serious eye troubles are not uncommon.

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Ocular Leprosy, with Reference to Certain Cases Shown

By D. P. Choyce, F.R.C.S.

I should like to record my thanks to Sir Neil Hamilton Fairley, Sir George MacRobert and Professor A. W. Woodruff for permission to demonstrate their cases.

I have had experience of two contrasting types of case: first, the detailed and repeated observation of 30–40 cases of leprosy in this country; about half of these have ocular involvement. Also, having been fortunate enough to travel fairly extensively abroad, I have superficially examined several thousand inmates of leprosaria in Malaya, India, Pakistan, Egypt and East Africa. It is more difficult to draw conclusions about this type of case, partly because there has never been a corneal microscope with which to examine them, and partly because so many of them have had other ocular disease. An interesting feature of many of these cases was corneal and conjunctival anæsthesia due to involvement of the V nerve, so that the trichiasis caused no symptoms and the patients, therefore, refused to submit to surgical correction of the trichiasis, with continuation of the damage to the cornea: an interesting example of the difficulties confronting the tropical ophthalmologist.

(1) *Nerve involvement.*—(*a*) The upper division of the VII nerve is not uncommonly involved in non-lepromatous leprosy, leading to myo-atrophy of the superior part of the orbicularis oculi. This leads to characteristic loss of "winking" and blinking, lagophthalmos, ectropion of the lower lid, and later, to exposure keratitis. In this connexion it is interesting to observe how much exposure the cornea can stand in these cases, and it is wise to delay tarsorrhaphy as long as possible.

(*b*) Branches of the V nerve may also be thickened and palpable, and corneal anæsthesia may be pronounced. Under these circumstances corneal ulcers readily form, cause remarkably few symptoms, and take a long time to heal.

(2) *Lids and lacrimal apparatus.*—In lepromatous leprosy madarosis (loss of eyebrows and lashes)

is common and is thought by some to indicate certain involvement of the eyeball itself, but this is not necessarily so. On the other hand, when the eyeball is involved, madarosis is usually, but not invariably, present. When present it is permanent, so that female sufferers frequently provide themselves with artificial eyebrows. Lepromata of the upper lid occur, but are rare in the lower. Absence of madarosis is a good prognostic sign in long-standing cases. Involvement of the lacrimal gland has been recorded but is not serious. Dacrocystitis, secondary to collapse of the nasal cartilages, is common, but usually due to pyogenic organisms rather than to Hansen's bacillus.

(3) *Involvement of the eyeball itself.*—In 1873 Bull and Hansen suggested that the globe became involved exogenously, i.e. that the bacilli were deposited in the lids or conjunctiva, and thence invaded the eye. This theory has been heavily criticized in recent years; Shionuma (1940) demonstrated leprous changes within the eye before bacilli appeared in the conjunctival sac. Fuchs (1940) suggested that the bacilli were deposited by the blood stream either in the episcleral tissues close to the limbus (whence they migrated into the cornea with the corneal nerves), or in the ciliary body. From the latter site they could spread forwards into the iris causing miliary lepromata, medially into the ciliary processes or posteriorly into the choroid causing chronic, destructive uveitis. In support of his theory Fuchs cites the well-known tendency of the tubercle bacillus to metastasize by the blood stream. While his assertion that clumps of leprosy bacilli are deposited in the limbal episcleral tissues and in the ciliary body may well be correct, it does not follow that they are conveyed thither by the blood stream. In view of the known predilection of the leprosy bacillus for peripheral nervous tissue an alternative, and to my mind reasonable, theory is that they migrate to these regions along the ciliary nerves. However they reach their destination, it is a fact that Hansen's bacilli cannot always be demonstrated in the conjunctiva in cases with leprous involvement of the anterior segment.

With regard to the macroscopic details, lepromata of the conjunctiva are rare; episcleral nodules occur but do not usually persist. The limbal region is frequently the seat of a characteristic sclerosing keratitis, involving the whole circumference. Nodules which superficially resemble pterygia may encroach upon the cornea.

The cornea itself is very frequently involved; the bacilli appear to reach it along the corneal nerves. All varieties of keratitis are encountered, but vascularization is very late. Pannus is usually confined to the upper segment, but may extend right round the cornea. It is distinguished from trachomatous pannus by the absence of involvement of the tarsal plates, abundant anastomoses between the vessels, and a lesser degree of infiltration of the substantia propria.

The iris is attacked in a number of ways. The most characteristic sign, never seen in any other condition, is the appearance of miliary lepromata near the sphincter in the deep mesodermal layer, between the frill and the pupillary margin. These lepromata have been shown to contain thousands of bacilli, with very little cellular reaction from the host. They may persist unchanged for years, causing little or no reaction, apart from slight atrophy of the stroma. Or the iritis may be acute with marked symptoms. Secondary glaucoma is frequent and of great danger to the patient, as it is this complication which is, in part, responsible for the high incidence of blindness in ocular leprosy. In this type of case complicated cataracts are a common sequel, and although lens extraction is practicable, the results tend to be disappointing. Finally, the iritis may be chronic and insidious and the patient may be unaware of eye changes until visual loss from atrophy of the ciliary body makes itself evident.

While iritis may be associated with antecedent corneal or iris changes, this is not necessarily so, and cases of severe iritis in an eye otherwise unaffected by the disease are often seen. Here it is reasonable to assume that the uveal tract has been sensitized in some way to the breakdown products of this disease, responding with an acute plastic iritis. Exacerbations of this nature can occur at any stage of the disease, even in the so-called "burnt-out" cases, and can be most alarming, calling urgently for expert ophthalmic attention.

With regard to the posterior segment, most authorities agree that such lesions are rare. Personally, I have never seen a choroidoretinal lesion which I was satisfied was due to leprosy and not due to syphilis, tuberculosis or some other intercurrent disease. Elliott (1948, 1949), of the United States Marine Hospital at Carville, firmly believes in the existence of these lesions which are said to be identical with those seen on the iris, and in the cornea. He states that these pearl-like lesions recede within eight months, leaving no trace behind. He may be right, but his observations so far as I know have not been confirmed by other workers. Pathologically, bacilli can readily be demonstrated in the ciliary body, occasionally in the anterior part of the choroid, but not at all in the retina.

There are some general points which need emphasis:

(1) Ocular lesions are common in lepromatous leprosy, almost unknown in the tuberculoid variety. Thus the incidence of these complications varies markedly geographically according to the type of disease prevalent. Broadly speaking the incidence of ocular leprosy is low in India, high in Europe, Japan and certain parts of Africa, and particularly high in Central and South America.

(2) Blindness is chiefly due to involvement of the iris and ciliary body either from gradual atrophy leading to phthisis bulbi, or from the less common but more dramatic secondary glaucoma. The corneal lesions play a subsidiary part in the causation of blindness.

(3) The ocular lesions are often of striking bilateral symmetry, thus lending themselves to clinical research in which one eye is treated on different lines from its fellow, which acts as a control.

(4) It is primarily an anterior segment disease, in which the bacilli are very numerous and the tissue reaction minimal, the only exception being some of the cases of plastic iritis.

(5) Eyes afflicted with ocular leprosy stand up surprisingly well to surgical procedures, such as lens extraction, provided the disease is in a quiescent phase.

This brief review of the clinical signs will now be illustrated by reference to some cases.

Case Reports

Case I.—Mrs. G. A., aged 40.

Anglo-Indian. Lived in India until 1947. No known contact with leprosy.

1943: Severe burns of hands. Noticed absence of pain. Since then she has had repeated burns of hands and legs due to cooking on an open fire, and has noticed gradual loss of digits and development of ulcers on soles of feet.

April 1953: Admitted to Hospital for Tropical Diseases. Found to be suffering from advanced lepromatous leprosy with destruction of nasal cartilage, hoarse voice from laryngeal involvement, loss of fingers and toes, analgesia of limbs, gross sepsis of right leg, unhealed burns of legs, and trophic ulcers of feet. Surgical treatment was carried out and treatment with D.D.S. (diaminodiphenylsulphone) was commenced.

Progress.—Clinical improvement has been good but bacteriological improvement has been slow. She has now had one and a half years' treatment.

Ophthalmic manifestations.—

1952: Bilateral naso-lacrimal obstruction due to destruction of nasal cartilages. Right dacrocystitis, controlled by penicillin and Albucid.

1953/1954: Occasional attacks of allergic iritis including one severe attack with secondary glaucoma. Controlled with mydriatics and cortisone locally. Systemic cortisone necessary for two days. No other stigmata of ocular leprosy. *Visual acuity* = 6/6 pt., 6/9 pt.

Comment.—This case shows: (1) The effect of destruction of nasal cartilages on the naso-lacrimal ducts. (2) Allergic iritis, satisfactorily controlled by mydriatics and cortisone.

Case II.—Mr. A. B., aged 39.

English. Was in various parts of the tropics (Army) from 1938–1943. No known contact with leprosy.

1949: Onset of erythematous macules on the skin.

1951: Nasal symptoms and epistaxis.

1952: E.N.T. specialist found a positive W.R. Venereologist was able to rule out syphilis on the strength of a negative treponemal immobilization test. A skin biopsy revealed very large numbers of acid-fast bacilli, and he was referred to the Hospital for Tropical Diseases in October 1952. Commenced treatment with a combination of Sulphetrone injections and I.N.H. (isoniazid), and this has recently been changed to D.D.S.

Progress.—Clinical improvement has been good but bacteriological improvement has been slow. He has now had two years' treatment.

Ophthalmic manifestations.—Has been observed for two years.

1952: N.A.D. Commenced sulphone therapy.

1953: Early superficial punctate keratitis above and early leprous pannus.

1954: I.S.Q., or possibly slight intensification of corneal appearances. No symptoms. *Vision* = 6/6, right and left.

Comment.—A case where minimal ocular involvement has occurred while patient is on systemic sulphone treatment.

Case III.—Miss E. K., aged 37.

Anglo-Indian. Lived in India until 1951. No known contact with leprosy.

Early lesions of leprosy appeared in 1950 and the disease has made a steady advance ever since. She is now an advanced case of lepromatous leprosy. She was admitted to Hospital for Tropical Diseases at the end of August 1954 and we are attempting to improve her nutrition and her anæmia before commencing treatment with sulphones. She is mentally deficient.

Ophthalmic manifestations.—A new case.

August 1954: Marked madarosis of eyebrows and lashes. Episcleral nodule, left temporal region. Marked leprous keratitis, punctate and sclerosing. Irides normal with loupe. Patient mentally defective and visual acuity impossible to determine. Put on atropine drops, right and left.

September 1954: One month's general hygiene (e.g. personal cleanliness, teeth, cleansing of necrotic areas) and treatment of anæmia has greatly benefited the ocular condition. Episcleral nodule almost healed.

As yet no systemic sulphone therapy.

21.9.54: Left conjunctival snip shows: numerous Hansen's bacilli.

Comment.—Gross corneal and limbal leprosy, with marked improvement with general hygienic and medical measures.

Case IV.—Mr. A. D. W., aged 24.

Anglo-Indian. Lived in India until 1947. No known contact with leprosy.

Between the ages of 7 and 15 he noticed slowly increasing sensory loss on the skin of hands, arms and feet. At the age of 16 he developed a trophic ulcer on the sole of the right foot, and three years later (1949) he noticed redness of his eyes and nodules appearing on face and backs of hands.

September 1950: Diagnosis of leprosy was made in Liverpool and treatment with D.D.S. was commenced.

July 1952: Developed sudden blindness in left eye.

September 1953: Admitted to Hospital for Tropical Diseases (Jordan Hospital, Surrey) where treatment with D.D.S. has been continued.

Progress.—Skin lesions have virtually disappeared and bacilli are slowly decreasing. Sensory impairment over arms, feet and legs has remained, and there is slight weakness of the right little finger. He has now had four years' treatment.

Ophthalmic manifestations.—

1951: On systemic sulphone therapy.

1952: Left vitreous hæmorrhage. This gradually cleared, revealing an extensive simple retinal detachment nasally. Right and left marked leprous keratitis and sclerosing keratitis. Right and left irides show some atrophy with numerous *miliary lepromata*, mainly above. No iritis. Media clear and fundus normal.

1953: No change.

1954: Possibly slight intensification of ocular changes, notably pterygium-like nodule of the right limbus at 9 o'clock, although systemic response to sulphones is good.

Comment.—(1) Severe ocular leprosy, yet: (2) no madarosis, (3) no iritis, despite miliary lepromata ++, (4) no fundus lesion. *Visual acuity* = 6/6 right; counts fingers, nasal field left.

Case V.—Mr. M. F., aged 70.

South African. Has spent most of his life in South Africa and in South America. No known contact with leprosy.

In 1938 he was diagnosed as suffering from lepromatous leprosy and treatment with hydnocarpus oil was commenced. In 1946 treatment was changed to sulphones, and the disease has been completely arrested. He is still taking D.D.S. He has sensory loss of the skin of feet, legs, hands and forearms, and there is a partial dropped foot (right) following an attempted biopsy of common peroneal nerve.

Ophthalmic manifestations.—

1948: Madarosis. Severe bilateral iritis with secondary glaucoma in right eye. Iritis presumably of allergic origin as no other stigmata of ocular leprosy present. No cortisone available at that time. Mydriatics insufficient to control tension. Iridectomy necessary.

1949/1954: Gradual intensification of complicated cataracts. Accurate light projection both eyes. Patient very anxious for something to be done.

June 1954: Right separation of posterior synechiæ and intracapsular extraction. Eye stood the operation well, but visual result disappointing. Optic disc pale. *Right Visual Acuity* = 2/24 with + 9/+3 ↓ 90, in lower nasal quadrant only. *Left visual acuity* = 2/60 unaided, not improved.

Comment.—This case illustrates the severity of the allergic iritis, and how pre-cortisone measures were not adequate to deal with it. Also that a major surgical intervention can be withstood by such a badly damaged eye, but that the visual result is likely to be disappointing.

Case VI.—Mrs. L. L., aged 30.

Anglo-Indian. Lived in India until January 1947. No known contact with leprosy. Treated for leprosy in India in her youth and discharged apparently cured.

1947: Nodules gradually reappeared over the next three years, and, by the time she was sent to the Hospital for Tropical Diseases in October 1950, she was an advanced case of lepromatous leprosy. Treatment was commenced with Sulphetrone injections and later she was transferred to the Jordan Hospital, Surrey.

Progress.—Her progress has been interrupted by frequent recurrences of reactional phases characterized by fever and erythema nodosum leprosum necessitating stoppage of treatment, and now she is on 50 mg. cortisone daily while continuing parenteral treatment with D.D.S. in the form of Avlosulfon Soluble. She has made considerable clinical improvement, however, and there are half as many bacilli in the skin as compared with 1950. She has now had four years' treatment.

Ophthalmic manifestations.—

1951: Left episcleritis with nodules. Systemic sulphone therapy.

1952: Left episcleral nodule smaller and asymptomatic.

1953: I.S.Q.

1954: I.S.Q. The episcleral nodule temporally has hardly changed in two years of systemic sulphone therapy. Asymptomatic. *Vision* = 6/6, right and left.

Comment.—While this case has improved it has not been cured; it is probable that if this patient had not received systemic sulphone therapy the ocular involvement would be very much greater than it is to-day.

Treatment

(1) *General hygiene and medical measures*, designed to eliminate septic foci such as teeth and secondarily infected areas of necrosis and to deal with any secondary anæmia, may have a beneficial effect on the ocular lesions.

(2) *General treatment of leprosy.*—The introduction of sulphones used systemically raises certain questions concerning the ocular complications of the disease. In view of the extreme chronicity of leprosy and the comparatively short period that has elapsed since this group of drugs was first used, it will be several more years before precise answers can be given.

(*a*) Do the sulphones prevent or delay the occurrence of ocular complications? In view of their markedly beneficial effect systemically, the common-sense view is that these drugs are more likely to prevent, mitigate or delay ocular complications than any previous systemic therapeutic measures used in leprosy.

(*b*) What effect do the sulphones have on established ocular leprosy? In several of my cases shown at this Meeting the signs have been arrested, in others partial regression appears to have taken place, but in none can it be said that complete cure has occurred. Furthermore, the ocular condition of one case (A. D. W.) appears to have deteriorated slightly while his systemic disease has improved. It is probably safe to say, however, that even if these cases are far distant from cure, their ocular state would to-day be appreciably worse in the absence of sulphones given systemically.

(3) *Local treatment of the eye.*—So far, there have been no reports of the use of sulphones locally, in the forms of drops, ointment or by subconjunctival injection. This problem is engaging our attention at the present time. Various gold preparations have been used locally, but reports of their effects are conflicting. The antibiotics are of use in restricting any secondary infection, e.g. of an obstructed lacrimal sac.

The local treatment of the plastic iritis, the most dreaded ocular complication of leprosy, is of the first importance. Mydriatics, reinforced by early local use of cortisone, represent a great advance in the management of this condition. Colonel Kirwan and I have successfully treated a number of these cases, who still retain a visual acuity of the order of 6/6–6/9, who would otherwise probably be seeing less than 6/60. Leprosy bacilli are noted for their sluggish powers of reproduction and in the eye for the minimal fibroblastic reaction they provoke, which probably explains the fact that we have, so far, seen no evidence of multiplication of the bacilli beneath the cortisone umbrella.

Prognosis

Twenty to thirty years ago a dissertation on leprosy would have included the statement that the ocular complications progressed remorselessly towards blindness, being unaffected by any known therapeutic measures. I have personally noted while abroad a certain apathy and want of interest in the treatment of ocular leprosy, engendered, no doubt, by the onward march of the disease. While the word "cure" can still not be applied to leprosy, I would suggest that it is now possible to talk of delaying the progress of ocular leprosy with systemic sulphones and that a proportion of the blindness associated with the disease can be prevented by the timely use of cortisone.

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Ocular Leprosy

By Lt.-Col. E. W. O'G. Kirwan, C.I.E., M.D., F.R.C.S.I.

In tropical countries leprosy is one of the great causes of blindness and partial loss of sight. There is no disease that has been so greatly dreaded through the ages. Horrible to live with, difficult to die with, slowly destroying the nerves and marrow, causing deformities and mutilations and finally, to complete the holocaust, often causing blindness. Thanks to the researches of a number of specialists in more recent years, we now possess in the improved treatment and better knowledge of the epidemiological conditions under which leprosy infections arise, the means greatly to reduce and eventually, we hope, to eradicate this terrible disease.

More than three million cases of leprosy are supposed to exist in the world, the great strongholds being India, China and Central Africa. India has a million or more cases and it is calculated that 15,000 children develop the disease annually. The first fifteen years of life is the period of highest contagion and especially the period 5–15 years. The incidence of the disease is greater in low-lying, humid areas in which the climate is hot and the rainfall heavy, rather than in more elevated dry ones. Great Britain is responsible for a very large number of patients in her colonies and only a small proportion are as yet receiving the benefits of established treatment.

It is difficult to determine the extent of leprosy in these islands in the past but at present there are about 150 cases in England and Wales. All these patients acquired the disease outside the country. Many cases seek refuge here and the disease is not easy to detect. The last British leper whose infection could not be traced directly or indirectly to the tropics died in 1897 in the Shetland Islands.

All the changes that affect the body in leprosy can affect the eye and its adnexa, and so the ocular manifestations have no mystery of their own. As in the body, the disease is one of relentless chronicity and presents very serious complications.

Ocular involvement is common but varies tremendously in different countries and amongst different races. The gravity of this involvement is directly dependent upon the type of the disease.

In the lepromatous type the eye complications are serious and caused by actual leprous infiltration both superficial and deep. In the non-lepromatous type, in which the peripheral nerves are involved, there is no actual leprous lesion of the eyeball. The branches of the VII nerve are frequently

involved, giving rise to lagophthalmos from myo-atrophy of the orbicularis oculi muscle. In the tuberculoid type the eyes are not involved except in those cases in which tuberculoid lesions are situated in the vicinity of the eyes. In these cases, madarosis, mild conjunctival congestion, hypo-æsthesia and anæsthesia of the conjunctiva occur.

Proportion of Ocular Involvement

While all writers agree as to the great frequency with which the eye is affected, there is a wide difference in the statistics of various countries and climates. Ocular involvement varies from 10% to 100% when the different forms of the disease are taken into account and if the adnexa are included it may be assumed that in the predominantly lepromatous type all but those in the first few years of the disease have involvement about the eyes.

The longer the duration of the disease, the commoner are the ocular complications, and it is probably correct to say that if the patient lives long enough and the disease persists, some form of ocular leprosy will eventually occur.

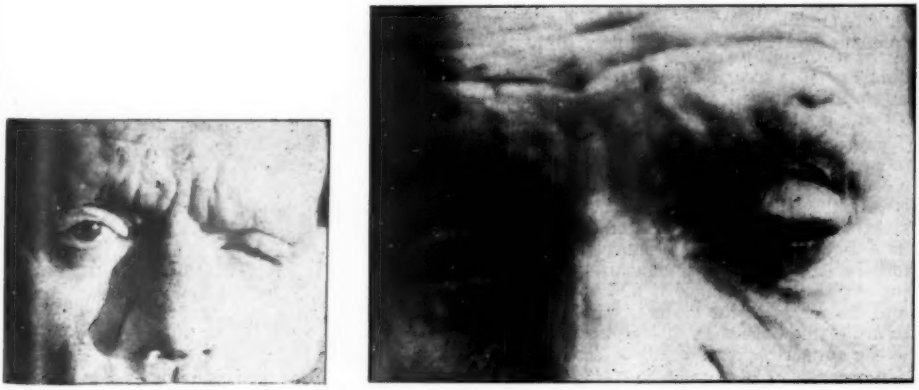
The wide difference in the occurrence of ocular complications can partly be explained by the fact that the surveys are not carried out by ophthalmologists. Early ocular involvement can often only be diagnosed by examination of the eye with the slit lamp and corneal microscope. The factor of time must also be taken into account as eye complications, as a rule, do not occur in the first few years of the disease. Time alone will decide whether the good results of sulphone treatment will lower the percentage of ocular complications.

Distribution of Ocular Lesions

The Superciliary Region and the Eyelids

Alterations of the superciliary region and the eyelids comprise madarosis, lepromas, infiltrations, macules, anæsthesia and lagophthalmos. They are found in all the clinical forms of leprosy, are of very great importance not only for the general diagnosis but also for the diagnosis of the type of the disease.

Madarosis, both superciliary and ciliary, is a very common sign, appears slowly or suddenly and usually during the first few years of the disease. It occurs in the lepromatous form, but also in the tuberculoid one, when it affects the forehead, in which case the rare unilateral madarosis is seen. It does not occur in the pure nerve form (tropho-anæsthetic variety). There is usually a close correlation between the degree of madarosis and the gravity of the eye lesions. The persistence of the eyebrows and eyelashes signifies that the patient is putting up resistance to the lepra infection and that involvement of the eyeball is still far distant. Lepromas occur on the margin and other points of the upper eyelid, but are never found on the lower eyelids (Fig. 1A and B).



A B

Fig. 1A and B.—Lepromas eyebrows, upper eyelids.

Lagophthalmos occurs in the non-lepromatous type and the expression that it gives to the patient's eye is pathognomonic. It is due to a slow and progressive process of myo-atrophy of the orbicularis oculi and may be unilateral or bilateral. It is generally preceded by fibrillary contractions of the eyelids. The palpebral fissure little by little becomes wider in proportion to the progressive weakness of the orbicularis oculi muscle. Later the superciliary and the frontal muscles may be involved. The lagophthalmos produces an ectropion of the lower eyelid with epiphora and later xerosis of the conjunctiva and cornea. Occasionally an ulcer on the lower third of the cornea may occur as

a result of exposure. Unless the lagophthalmos is accompanied by an anæsthesia in the region of the V nerve, diminution or loss of sensibility of the conjunctiva and cornea does not occur. The absence of reflex winking is due to loss of function of the orbicularis oculi and not to the loss of corneal sensibility. Once leprous lagophthalmos is established, it is usually permanent and will not recede, but despite the cornea being so much exposed, it is remarkable how so many of these cases escape corneal ulceration over a very prolonged period often extending into many years.

There is no disease of the lacrimal gland sac or duct peculiar to leprosy. Chronic dacryocystitis is, however, rather common, is secondary to the septic process present in the nose and frequently gives rise to blepharitis and purulent conjunctivitis. The lacrimal gland may be hypertrophied increasing the flow of tears.

The Conjunctiva, Episclera and Sclera

Mycobacterium lepræ has been found in the conjunctival secretion and in biopsies from the conjunctiva in clinically healthy eyes. Hyperæmia and congestion of the conjunctiva frequently occur. These may be diffuse or limited to a triangle on either side of the cornea. The conjunctiva plays a very important role in the transportation of the lepra bacilli. Being an exposed tissue like the skin, it can be infected directly, or more commonly, the infection spreads from the surrounding skin lesions.

Leprous nodules are never found on the conjunctiva as the bacilli do not proliferate in the conjunctiva but in the episcleral tissue and upon the surface of the sclera close to the sclero-corneal junction where the anterior ciliary nerves penetrate. They appear to have a marked preference for this area on account of its peculiar structure and position. Yellowish, gelatinous nodules appear in this area more usually on the temporal side. They extend around the limbus producing a low rampart of granulation tissue and eventually obliterate the whole contour of the limbus.

The infiltration spreads into the superficial layers of the cornea, destroys Bowman's membrane, and produces a sclerosing keratitis. An anterior staphyloma of the cornea may result. Hypoæsthesia or anæsthesia of the conjunctiva occurs in the lepromatous type and is of great value in diagnosis, as if it is found present it is a warning of impending serious ocular lesions.

Invasion of the conjunctiva, episclera and sclera are ordinarily not accompanied by great pain or acute reactions so that the patient delays in seeking medical advice.

The Cornea

The cornea is the most vulnerable of the ocular tissues and is very commonly involved. All varieties of keratitis are seen and can best be classified into primary and secondary. The primary comprise five groups—pannus, sclerosing keratitis, superficial punctate keratitis, deep or interstitial keratitis and leproma of the cornea. Lesions of the sclera and limbus precede or accompany the keratitis. The secondary ones comprise the ulcerative group which may occur in lagophthalmos and when there is loss of sensibility of the cornea. Pannus in leprosy is very common and presents itself in the form of a net, the meshes of which are composed of uniform branching blood vessels, in contradistinction to the pannus of trachoma in which the new blood vessels are terminal and arranged in the shape of bundles. It is seen in all stages from early vascularization in the upper third of the cornea to the severe forms in which there is deep vascularization as well. Grave forms are seen causing a partial or even complete hyperplastic keratitis.

Leprous sclerosing keratitis is a common occurrence, in which the sclerotic coat of the eye appears to invade the cornea. It occurs as a band of variable proportions with a very pronounced white colour and new blood-vessel formations are either absent or scarce. Superficial punctate keratitis is probably the most common ocular lesion in leprosy, is quite unlike other types of superficial keratitis and its presence is pathognomonic. It usually begins at the superior limbus as a light milky haze, punctuated by tiny white spots resembling grains of chalk and varying in size. These spots are miliary lepromas. The keratitis is accompanied by superficial vascularization and is not truly superficial; at the limbus it affects the deeper layers, but tends to remain superficial as it spreads into the centre of the cornea. The lower margin is delineated by a wavy line above the pupillary centre of the cornea so that vision at first is not impaired, but when the keratitis extends over the whole cornea the vision will be seriously and permanently affected (Fig. 2).

Interstitial or deep keratitis begins at the periphery of the cornea from extensions of pre-existing lesions at the limbus and the episclera. With the corneal microscope the opacities can be seen to be composed of small nodular infiltrations with new blood-vessel formations below Bowman's membrane in the superficial layer of the substantia propria and not affecting Descemet's membrane or the corneal endothelium. When it is limited to one sector of the cornea, vision is not much affected, but if it involves the whole of the cornea the vision will be permanently lost.

Another type of interstitial keratitis sometimes seen is the degenerative circular keratitis that extends around the entire corneal circumference. It simulates the peripheral annular lipoid infiltration of the corneal stroma so commonly seen in elderly people especially in those who have lived in the tropics and known as arcus senilis. The superficial and deep forms of keratitis are often seen in combination and are usually bilateral.

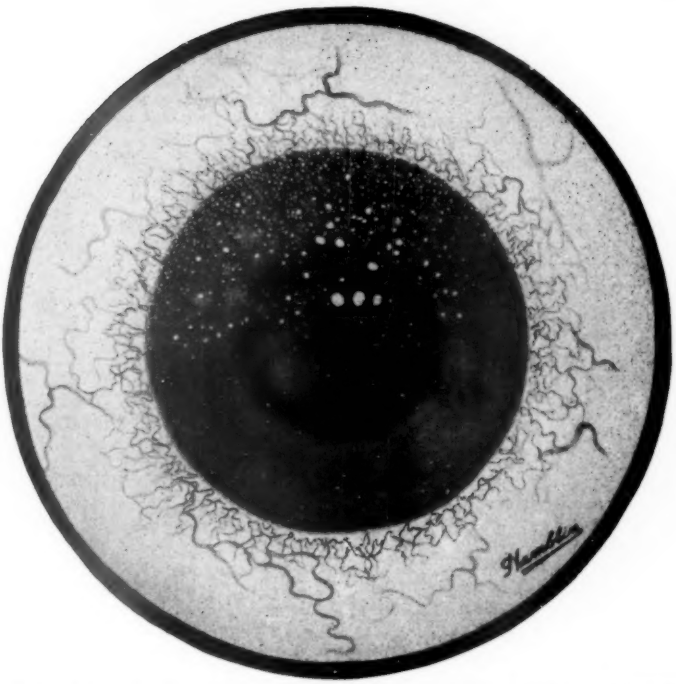


FIG. 2.—Leprosy—showing characteristic pannus and superficial punctate keratitis.

A leproma of the cornea is never primary, but commences at the limbus and in its early growth into the sclera and cornea resembles a pterygium carnosum or vasculosum. It may be solitary and grow to a large size even impeding the closing of the eyelids. It is smooth, reddish in colour and the conjunctiva over it is adherent and mildly congested. The nerves of the cornea may be prominently seen in some cases and are thickened or beaded.

The Iris and the Ciliary Body

Second only to the cornea, the iris and the ciliary body are the parts most frequently involved and usually occur as direct extensions from the sclera. Involvement of these tissues is the commonest cause of blindness.

Four types may appear:

(1) The serous or plastic type is the most frequent and is characterized by its insidious onset and relentless chronicity. In the early stages the eye is relatively quiet and the only symptom is the gradually decreasing visual acuity. In the beginning the synechiæ are very few and are only discovered by the corneal microscope or atropine. They slowly grow and may involve the whole pupil circumference. The signs of plastic iridocyclitis are often present as well: i.e. keratitic precipitates on the whole of the corneal endothelium; exudates on the anterior lens capsule and anterior chamber; irregularity of the pupil and multiple posterior synechiæ (Fig. 3). All the graver manifestations may be observed—posterior synechiæ with seclusion and occlusion of the pupil, secondary glaucoma, vitreous and lens opacities, hypotension, retinal detachment and atrophy of the eyeball.

(2) An acute diffuse plastic iridocyclitis of sudden onset somewhat similar to the ordinary non-specific acute iridocyclitis but of a more violent nature is sometimes seen. In my experience it is not very common and is usually due to the lepra reaction in the eye and may be unilateral or bilateral. It is accompanied by very severe pain, lacrimation, photophobia, circumcorneal injection, extensive posterior synechiæ and exudation into the pupil and vitreous body. It usually results in blindness or great loss of sight.

Recurrences of the plastic type of iridocyclitis occasionally are seen even in patients who are cured or supposed to be cured of the disease. These recurrences are not due to the *Mycobacterium lepræ* and react well to atropine and cortisone drops.

(3) Miliary lepromas on the anterior surface of the iris are well seen with the corneal microscope, usually accompanied by the co-existing changes of superficial punctate keratitis. They are frequently

FIG. 3.—Leprosy—showing plastic iridocyclitis with miliary lepromas on the iris.

seen and are greyish yellow, pedunculated or flat, pin-point bodies scattered irregularly on the iris and on the exudates on the anterior lens capsule. They are characteristic and pathognomonic of leprosy and resemble the tiny white spots found in the cornea. They are liable to be overlooked unless the eye is examined with the corneal microscope. The iris tissue on which they rest either appears normal or is atrophied exposing the pigmentary layer. The signs of plastic iridocyclitis are often present as well.

(4) Nodular lepromas are much less common. They are yellowish in colour, globular, sometimes flattened, assume variable dimensions and have no fixed site.

In iridocyclitis the *Mycobacterium lepræ* is not found in the aqueous humour but occurs in large numbers around the blood vessels especially in the region of the circulus major. The aqueous contains small lymphocytes variable in size, some free and others lying in the exudate, large lymphocytes isolated or in groups and many histiocytes. The leprous process in the eye is characterized by the marked disintegration and migration of the iris pigment. In all varieties of iridocyclitis, atrophy of the iris is found in varying degree. The whole tissue gradually becomes dull and grey, the crypts disappear, the blood vessels become visible and finally holes appear.

Lesions of the Posterior Segment

Although ocular leprosy is characteristically a disease of the anterior segment of the eye, lesions of the posterior segment behind the ora serrata do occasionally occur by direct spread from the episclera, limbus, iris, ciliary body, anterior choroid, ora serrata and backwards. The wonder is that they are not more frequently observed. This may partly be due to the lack of observations of fundus changes due to the fact that their visualization is prevented by the degree of change usually found in the anterior segment of the eye. Polypoid lesions of the fundus have been observed in 6 cases by Elliott (1949). These take the form of small, waxy, creamy white and pedunculated nodules on the retina extending into the vitreous humour. 5 of the cases had leprosy for at least fifteen years and 1 case was of one year's duration. These lesions occurred in the lepromatous, tuberculoid and mixed types of the disease. Cases have been reported of choroiditis and lesions of the optic nerves before the anterior segment of the eye has become involved. At the same time it must be remembered that the *M. lepræ* has never been found in the choroid in histological examinations and it is probable that the choroiditis and optic nerve lesions were due to other concomitant causes such as syphilis or tuberculosis.

Pathogenesis of Eye Lesions

Leprosy is a systemic infection, and Hansen's bacilli are found in the peripheral blood. The lepromatous infiltration of the eye is part of the generalized infection. As lesions in the posterior segment of the eye do not occur—or at all events occur rarely—in marked contrast to syphilitic and tuberculous ones, so the portal of entry for ocular invasion in the lepromatous type is best explained by the transportation of the bacilli by the blood vessels or lymphatics from the lepromata on the face and eyelids to the conjunctiva, episclera and the anterior segment of the eyeball. There are, however, points in favour of the endogenous passage in which the uveal tract is first affected, beginning in the angle of the iris, spreading in front of the iris, inwards to the ciliary body, backwards to the choroid and outwards to the sclero-corneal limbus.

In tuberculoid leprosy, the conjunctiva being an exposed tissue may be involved when the skin around the eyes or on the face is affected.

Treatment of Eye Lesions

In leprosy, loss of vision is caused by changes in the cornea and plastic iridocyclitis. Up to the advent of the sulphones, treatment was fraught with disappointment, hydnocarpus oil, the ancient Eastern remedy, was up to that time the most reliable treatment and had retained its place for a very long time. In my experience the benefit to the eyes from sulphone therapy is remarkable but the early diagnosis of eye lesions and early treatment both local and general are of great importance. In incipient cases the specific lesions of the cornea and iris very slowly recede but not in advanced cases in which profound changes in the ocular tissues have already occurred, although even in the grave cases much can be done to prevent blindness. It takes three to five years for a lepromatous case to become negative. With sulphone therapy relapses do not occur or at all events it may be years before a relapse is detected. The case which tends to relapse is the tuberculoid one. This is determined by the ability or inability of the tissues to respond to the *M. lepræ* by a vigorous reaction. In the last ten years in which sulphone therapy has been employed for the treatment of leprosy cases in England, no case of blindness has occurred. In one case sight was seriously affected by acute iridocyclitis caused by the lepra reaction. No longer does one see the same amount of mucopurulent conjunctivitis, septic inflammation of the eyelids and chronic dacrocystitis which are so common in untreated cases of leprosy. Unfortunately with sulphone therapy there is a tendency to precipitate the lepra reaction in the early months of treatment and until it is controlled the eyes must be carefully watched in case the lepra reaction occurs in the eye. This is the most terrible ocular complication of leprosy. Great care therefore should be taken against injudicious or inadequate treatment. ACTH and cortisone, in spite of their immediate striking effects in the lepra reactions, have provoked a divided opinion. Some workers have got good results with small doses and others have found that cessation was followed by acute manifestations of leprosy and by increase in the underlying disease. The local application to the eye of cortisone in 1 per cent drops or ointment is most valuable in the acute eye conditions in which an unchecked inflammatory reaction will cause occlusion and seclusion of the pupil with secondary cataract and secondary glaucoma. It should be used frequently and continued till the eye is white. Cortisone, however, should be regarded only as an adjuvant to the sulphone therapy to lessen the danger of residual damage from an excessive inflammation. In lepromatous cases, the pupils should be frequently observed and if early signs of iritis are observed, the pupils should be kept well dilated by atropine. These early signs are often only discovered by the corneal microscope and one should always be available in hospitals where leprosy is treated. Unfortunately many of the patients one sees show the iris bound down by posterior synechiæ, the pupil small and filled with exudate so that atropine in these cases is of little use. If the pupil refuses to dilate sufficiently or if secondary glaucoma occurs, an iridectomy should be done. The leprous eye, despite the chronic inflammation, stands surgery very well.

Lagophthalmos is usually permanent if it has persisted for any length of time. I have seen one early case clear up with sulphone therapy. In view of the success obtained with cortisone in acute cases of Bell's palsy, it would perhaps be of value in accelerating recovery in early cases. Liquid paraffin drops should be instilled at bed-time to protect the cornea and if corneal ulceration occurs a tarsorrhaphy must not be delayed.

Summary

The ocular complications of leprosy are the most serious lesions in the disease. Leprosy has been one of the great causes of blindness and partial loss of sight. With the advent of sulphone and cortisone therapy, most of this could be prevented if only patients suffering from this disease received the benefits of established treatment in the early stages. There are thousands and thousands of people in backward countries suffering from leprosy who receive no care.

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Mr. E. F. King said that he could only speak from limited experience of ocular leprosy. He had, however, before the war seen a few cases at the Homes of St. Giles in Essex, and two years ago he had made a tour of East Africa and had visited a number of leper colonies in Uganda, Kenya, Tanganyika, and Zanzibar.

In visiting these leper colonies in East Africa he had been impressed by the relatively few cases showing ocular involvement. Moreover, when the eyes were affected, the lesions were usually gross in nature resulting in opaque corneæ, shrunken globes and staphylomata. He had discussed these cases with Dr. J. Ross Innes, the Leprologist to the East African territories, who had emphasized the point made by Mr. Choyce, that there was a great variation in the incidence of ocular involvement in leprosy in different parts of the world, and also in the type of eye lesion.

Mr. King had been told that at the commencement of sulphone therapy severe generalized reactions and exacerbation of iritis might occur, on the lines of the Herxheimer reaction. These effects could generally be controlled by systemic and local cortisone.

Dr. Robert G. Cochrane stated that, with the introduction of sulphones, a great deal could be done for ocular leprosy and the whole outlook had been changed for the better, particularly if treatment was commenced at an early stage. It should now be possible to prevent blindness, even though, under the older treatments if the leprosy of the eye were adequately treated, blindness could be staved off for a very long time. It was interesting to note that there appeared to be a difference in the incidence of eye lesions in the various races of the world. This difference seemed to be in some way connected with pigment, for if one divided the races of the world into lightly pigmented races and darkly pigmented ones, generally speaking, one would find that in the darkly pigmented race ocular leprosy seemed far less common. This was illustrated in his own institution in India, where there were a large number of Anglo-Indians and they showed a high incidence of ocular leprosy as compared to that seen in the Indian races. This statement also applied to the African races, where, by and large, ocular leprosy was not so serious, neither was the incidence so high as in the less pigmented peoples.

With the introduction of cortisone, serious effects of ocular leprosy could now be very largely prevented, and if cortisone were used very carefully then specific therapy could be continued. This, in the past, was always a great difficulty, because specific therapy had to be stopped when certain eye reactions showed themselves. While cortisone would benefit any eye reaction condition in leprosy, it was of most value in the so-called erythema nodosum reaction of leprosy, if, at the same time, careful sulphone therapy was given as well. Several of the cases seen at the meeting had passed through a period of very severe erythema nodosum. This phase eventually passed off and when it did the progress of the patient under treatment was smoother, and there was seldom a recurrence.

Dr. Cochrane confirmed the statement that it was the anterior part of the eye which was involved. He had never seen the posterior chamber affected. He did not think the changes described by Elliott had been confirmed by others.

The speaker added that he had been a little surprised to learn that Mr. Choyce was so relatively optimistic about operating. Personally, the speaker felt that if the eye was involved there was grave risk in operation. He did not advise this until the eye was quiescent unless the condition happened to be extremely serious, because so often interference set up changes in the eye and often when the eye was involved and the cornea also one tended to get opacities in the line of the incision. However, he was not an ophthalmologist, and he did not operate unless absolutely forced to do so. One had to be very careful before operating on an active lepromatous eye.

Dr. A. V. Clemmey spoke as one who had lived for twenty years in East Africa during which time he had seen little intra-ocular trouble; generally, it was a matter of keratitis and some anæsthesia. He had happened to see in Liverpool the case (Mr. A. D. W.), and in that case iritis had responded to atropine and cortisone.

Section of Neurology

President—Professor F. J. NATTRASS, M.D., F.R.C.P.

[*October* 7, 1954]

Recovery from "Muscular Dystrophy" [*Résumé*]

PRESIDENT'S ADDRESS

By Professor F. J. NATTRASS, M.D., F.R.C.P.

THE muscular dystrophies are generally regarded as incurable diseases, but a number of reports have appeared of spontaneous recovery in isolated cases believed to be of this nature. Of these reports some carry more conviction than others, the most impressive being those of Erb (1908) and Bramwell (1922). Erb's own comment was "I have never formerly seen recovery take place in a wide experience of such cases and did not consider it possible, but this case has taught me otherwise". The patient reported by Bramwell was regarded by most who saw him as the subject of typical pseudohypertrophic muscular dystrophy, but he made a complete recovery in the course of some three years.

Many cases have since been recorded showing improvement which has been attributed to a variety of therapeutic agents: but none of the recent papers contains any well-documented case of complete recovery. A therapeutic trial in 98 cases led to the conclusion that none of the principal remedies hitherto used has any influence on the course of true muscular dystrophy (Walton and Nattrass, 1954).

Eight cases are reported, all of which had recovered, either completely or almost completely, from a condition previously diagnosed by experienced observers as progressive muscular dystrophy. Reasons are given for supposing that two of these patients may have been suffering from a benign congenital myopathy and another from dermatomyositis. In the remaining 5 cases the clinical findings were characteristic of the childhood or Duchenne type of muscular dystrophy, save for the facts that one patient suffered two separate and distinct episodes of muscular weakness, and that in all five cases the onset of the disease was much more rapid than is usually the case in classical progressive myopathy. In two of these cases recovery was probably spontaneous but in the others improvement appeared to be related to the administration of wheat germ preparations.

Evidence is advanced that these five patients were suffering from polymyositis, a condition similar both ætiologically and pathologically, to dermatomyositis, save for the absence of skin involvement. Rapid progression of muscular weakness and a tendency to spontaneous remission are two features which may serve to distinguish this group of cases from those of true progressive muscular dystrophy. The pathological changes in muscle observed in polymyositis are very different from those of muscular dystrophy. Hence muscle biopsy is the only certain means of differentiation between the two conditions; this procedure should be carried out in any atypical or unusual case of proximal muscle weakness, since the prognosis of polymyositis is very much better than that of dystrophy, and improvement after treatment with ACTH, or perhaps, wheat germ preparations is possible.

This study was carried out with the co-operation of John N. Walton. The Address is published in full in *Brain* (Nattrass, 1955).

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The Future of Neurology

By Sir FRANCIS WALSHE, O.B.E., M.D., F.R.S.

As far as I can recall I have not had the privilege of making a communication to this Section for over thirty years, and if I now break silence here it is not because I believe that I possess some special insight into the future of neurology, by which I mean neurological medicine, but because I feel considerable anxiety for the future of a branch of medicine to which my professional life has so long been devoted, and grave doubt as to whether we are giving sufficient thought to the problems that surround it if it is to remain an active, advancing and fruitful branch of medicine.

I hope it will be clear that what I propose to discuss is neurological medicine itself and not the theme of the economic future of neurologists. I shall not put the cart before the horse.

Now it may seem absurd to you that I should feel these misgivings, and you may come to the conclusion that I am living in the past and have lost touch with what is happening around me in neurology.

"After all", you may say, "are we not hot upon the heels of every fresh advance in electrophysiology and applied electronics, using each new technique with conspicuous ingenuity, has not the application of this knowledge provided us with a diagnostic weapon of great value in the method of electroencephalography, produced a most voluminous and impressive literature, banded eager young men together all over the world in electroencephalographic societies, and, finally, given a half-title to a new journal, *Electroencephalography and Clinical Neurophysiology*?": a title wherein we see a technique taking precedence of a science in a manner so symbolic of the modern outlook, and so wanting in a sense of the ridiculous.

Let me put your minds at ease. Obviously, there are senses in which we are extremely up to date, and it is not my purpose this evening to dispute this, but rather to ask whether our enterprise is taking neurology in any clearly thought-out direction, and whether the time may not have come to ask ourselves about what is *not* going on in neurology.

For us, then, what is a relevant direction of advance? I have defined neurology as neurological medicine. The term has other references, but for the moment I am speaking as a physician charged with the care of the sick, responsible to the level of my knowledge and ability for the diagnosis and treatment of particular persons, and also, as far as the quest for new knowledge is incumbent upon me, responsible for seeking the causes and modes of development of nervous diseases, and for effective remedies for them.

In short, I submit that the primary research responsibility of the neurologist is to look for the causes and to seek the cure and prevention of the illnesses that come within his scope. Of course, this is putting the case crudely, but surely with a realism that it is not unfair to expect from us. What are we doing in this regard?

At once we encounter the problem of the modes of research and the branches of science involved if we are to achieve success in this most difficult task; yet one which is implicit in our profession: and this in turn brings us to the consideration of what have hitherto been the main lines that neurologists have followed in their original work and thought, and of whether these still remain adequate to the discharge of what I have called our responsibilities to the sick committed to our care.

I think it would be agreed that in the matter of original work, our principal interests and achievements have been, firstly, in the minute description and analysis of disease states and their correlation with the underlying pathological lesions, and secondly, and to an almost equal degree, in the fields of neuro-anatomy and neurophysiology.

It would also be accepted that our clinico-pathological discipline of itself indicates what is the effective treatment in some forms of illness, particularly those where the lesion is macroscopic and local. For example, the clinico-pathological identification of subarachnoid hæmorrhage, subdural hæmatoma, intracranial aneurysm and other vascular anomalies, by observers, physicians and surgeons, still active amongst us, has contributed greatly to the welfare of sufferers from these particular lesions.

Candour compels us to admit, however, that a century of nosography and morbid anatomy has left us with many crucial problems of ætiology and treatment wholly unsolved: as, for example, disseminated sclerosis, motor neurone disease, and various metabolic disorders of the nervous system, so painfully remind us and—let us not forget them—our patients.

When we come to the long and distinguished record of the clinical neurologist's achievements in anatomy and physiology, it is, I must submit, very clear that these disciplines, also, have not contributed widely or strikingly to the elucidation of the problems of ætiology, pathogenesis and treatment that confront us.

Clearly they must be an integral part of our training, but why have they also occupied us so exclusively in the field of original work, seeing that the direct attack upon the problems of ætiology is a primary responsibility of the neurologist?

I believe that a glance at the history of neurology explains this state of affairs. To read the contemporary literature of the 1870s is to feel again the excitement that the discoveries of the pioneer physiologists, Fritsch and Hitzig and Ferrier, gave rise to in neurological circles. Some of our ablest clinicians then and for many years gave themselves not only to clinical but also to animal experimental studies, and with great distinction.

Thus clinical neurology took, as it were, the prevailing anatomical and physiological colouring of the age, and neurologists came to feel pride in association with a science so highly regarded as neurophysiology became and yet remains.

This sentiment and the fascination the subjects must have for the neurologist have together led us to assume—if never clearly to postulate—that research in the anatomy and physiology of the nervous system was what was most needed from us and was our obvious mission.

So to-day we see that this eagerness to engage in the problems of neurophysiology, by the new methods that the ingenuity of the electrical engineer has made possible, still grips the imagination of many of the younger generation of neurologists, and if now I am to suggest that, even when pursued by the newest devices, this discipline yet still fails to make any major contribution to the solution of the pressing problems of disease that face us, I shall doubtless invite a vigorous protest from some of my listeners. Yet this is precisely what I do suggest for your most careful consideration.

Furthermore, although for many years the neuro-anatomical and physiological were—or seemed—the only lines of research that had a clear relevance to neurological medicine, in the past twenty years there has been a profound expansion in the variety of scientific resources open to us. In the world of general medicine, from which we too easily become remote, we have seen during this period a rapidly increasing application of the chemical sciences. Inorganic and organic chemistry, metabolic and enzyme studies have been and are the means by which discoveries of moment are everywhere being made.

Therefore, while the study of the structure and the dynamic activities of the nervous system must always be an important element in the formation of the neurologist's mind, these subjects can no longer continue to be the principal field of his research activities, or his chief tools in the approach to the problems of disease: partly because they are largely irrelevant to his primary responsibilities, but even more because we now have other scientific disciplines that offer hopeful prospects for research of a kind from which at last our patients may derive greater advantages.

Whoever intrudes a new point of view upon this most conservative branch of medicine has to guard himself against misunderstanding. Let me repeat, therefore, that although clinico-pathological study leaves so many of our problems unsolved, it must remain the foundation of clinical neurology and secondly, that I am not proposing that we should cease to study the anatomy and physiology of the nervous system in favour of some other basic sciences.

My point is that each of these is of its nature an incomplete mode of understanding. Even all three together are still limited in the light they are able to throw upon our disease problems. If we confine our activities to them, or allow the exclusive or excessive use of any one of them to become a vested interest, they can be obstructive nuisances on the path to knowledge in that they keep us from wider studies and dissipate our human resources.

Again, we may not forget that in Newman's sense, ours is not a liberal profession: that is, one pursuing knowledge for its own sake—science for the sake of science—as are the professions of anatomist and physiologist. We seek knowledge for a practical end. To anatomist and physiologist morbid categories are of little significance, to us they are our primary concern.

I submit, therefore, that the time has come to make a balanced and comprehensive review of what our research responsibilities have now become: one not tied to obsolete and conventional notions of what kinds of research it is becoming for us to do.

We have never attempted anything of the kind, and our activities remain individual and uncoordinated, we are without general principles and follow no common aim. We lack clear ideas familiar to us all of what is necessary to make neurological medicine ever more effective for the control of those diseases, the occurrence of which alone gives purpose and meaning to our activities.

Surely the crying need for such a survey is apparent when we come to consider our very modest therapeutic achievements.

All major contributions to curative treatment—apart from those we owe to the neurosurgeon—have come to us, not from the neuro-physiological laboratory, nor from the clinical neurologist, but from workers and laboratories not primarily concerned with diseases of the nervous system.

We have indeed gratefully to acknowledge the contribution of the surgeon, even though it covers but a small part of the whole field of neurology. Yet who shall say that it has yet reached its limits?

While we realize that it was clinical acumen together with a knowledge of the anatomy and physiology

of the nervous system that in 1900 enabled Russell, Batten and Collier to identify and analyse the symptom-complex of subacute combined degeneration of the spinal cord, we yet know that this malady continued to be uniformly fatal for twenty-six more years until workers outside neurology, and not using our two basic sciences, determined the ætiology and provided the effective remedy.

Need I remind this audience that there yet remain common as well as rare affections of the neuromuscular system that we have identified, described and interpreted that nevertheless are still as completely beyond our control as when clinical neurology first emerged as a separate discipline a century ago?

Yet so remote from the systematic study of these disease problems does much of our research remain that one has to ask whether we still look to the electrode or the amplifying valve as the Delphic oracle that is going to reveal to us the secrets of disseminated sclerosis and of those other disabling maladies the behaviour and incidence of which we do not know how to influence.

Of course this is a rhetorical question, and as such may be thought to need no answer, but its implications will not be lost upon anyone who sees the preoccupation with electrophysiology that dominates so much research and routine work amongst us, almost to the exclusion of other orders of enquiry. Was it not, indeed, upon the wall of the temple at Delphi that the words were written, "Nothing too much"?

Now the proposition that the clinical scientist should fit himself to conduct research in whatever scientific discipline is relevant to his problem in medicine, and that he cannot leave this to the non-medical expert, has been so cogently argued by two of the great figures in modern medicine, Wilfred Trotter and Thomas Lewis, that it ought not to be necessary for me to take up this point, and I should be able to assume that my listeners are familiar with the relevant essays in Trotter's "Collected Papers" and Lewis's "Research in Medicine".

Yet, some neurologists hold that while it is proper and needful that we should engage in high-grade anatomical and electrophysiological studies, it is unnecessary and unreasonable that we should have to do the same in any other field of natural science, for example, biochemistry. This view is without logic and has no rational basis. It derives from conservatism and lack of vision. All round us in medicine we find physicians working in chemistry and biochemistry, or in any discipline that may be needed to elucidate the medical problems upon which they are engaged.

Yet, in the present state of neurological opinion I tremble for the fate of a young man who, having served an apprenticeship to clinical neurology, turned to two or three years' study in some aspect of biochemistry so that on return to clinical work he might more effectively engage upon ætiological studies of disease. He would probably find the narrow gate of neurological opportunity closed to him, while, behind his back, some more worldly-wise young man had slipped through it along the well-worn track of electrophysiology and safety first.

I submit that if we prove less versatile than our colleagues in internal medicine there can be no future for neurology. We may not opt out of the wider applications of science. Those whom we must train for research in neurology will not all wish to follow the same scientific discipline, but some of them, and these, I believe, the most far-seeing and courageous, will want to explore the new fields so that they make some contributions to the understanding of disease.

It is an illusion to believe that the pure clinician, skilled in none but clinical methods, can any longer engage in fundamental research into this problem, or that, like a superman, he can control and direct the work of non-medical scientific experts the nature and possibilities of whose disciplines he does not understand.

At the Lisbon International Neurological Congress in 1953 there was a symposium on metabolic disorders of the nervous system, introduced by Dr. van Bogaert in a paper of great erudition. I quote his final passage in free translation: "Nosography and the classical histological methods can take us no further in the study of the lipidoses. Their genetic analysis has told us all it has to tell. Between the neural and the non-neural aspects of the disease there is an unbridged gap, and our questions as to the nature of the humoral disorder receive no answer because they need a more exact knowledge of the chemistry of metabolic disorders than we possess." He was followed by Dr. Klenk, who said, "I am certainly telling you nothing new when I commence my report with the statement that from the chemical point of view our knowledge of the lipidoses is very limited".

Of how many other affections of the nervous system might not the like be said? Is this no concern of ours?

Indeed the study of metabolic disorders has never effectively challenged amongst us the supremacy of morbid anatomy. No current textbook of neuropathology deals with anything else than the microscopic lesion, and the biochemical lesion might not exist as a relevant concept. In one standard textbook, the revealing subtitle is, "A study based upon a survey of lesions found in forty thousand autopsies".

Such contributions as we have to a dynamic, experimental, neuropathology come from outside our ranks or from the occasional neuropathologist who has for a while left the histologist's bench to contemplate pathological process, as a change from forever gazing upon pathological debris.

That morbid anatomy and histology have made a fundamental and essential contribution to neurology no one disputes, but to continue to regard neuropathology as concerned solely or even mainly with what can be seen in a microscope or a post-mortem room is at this time a narrow and obsolete view.

In the general tendency to look narrowly upon our problems I think it is possible to discern one significant factor. The nervous system that we have so long studied under the dominating influence of the physiological and the biophysical approach is an abstraction, and we have forgotten all that has been left in the discard.

We have thought of the neurone only in respect of its specific function, of what goes on at its surface and at its planes of synaptic contact: just as the biophysicist or the small current engineer regards it. We overlook that behind this wall, as it were, the neurone is not a vacuum but a living cell like every other cell in the body in that it has what I may call its private life: its metabolic, respiratory and its enzyme activities: a dynamic complex that is an integral part of that total activity that is the organism: for in the last resort, the neurone—like the entire nervous system—has no autonomy, and would be meaningless if it had.

My submission, then, is that we should ask ourselves three questions vital to the future of neurological medicine: firstly, what are our primary research responsibilities, secondly, what orders of research are best calculated to meet them, and thirdly, what range of training in scientific disciplines must we make it possible for our young men to obtain?

We all realize that even the best designed and executed researches do not always provide the answers we seek, but this fact does not absolve us from the obligation of foresight and wisdom, and it seems to me clear that our research outlook must be re-oriented: pride of place must pass from electrophysiology to a dynamic and experimental neuropathology employing whatever scientific methods may be necessary.

Conscious of this situation as it affects medicine in general, the Medical Research Council has recently created a number of scholarships which allow the trained young clinician of promise to obtain three years' training in a scientific discipline relevant to the field of work he intends later to cultivate as a clinician: the last of the three years being devoted to the application of what he has learned to medicine.

I know of no other kind of administrative measure that can meet the need which, in respect of neurology, I am seeking to bring to your notice,

Of course, I am not alone in seeing the need for a broader-based neurology, but in general when we glance at the waters of neurological medicine they are so calm that they do no more than reflect back to us the complacent expressions with which we gaze upon them. This is why I am here to trouble the waters.

I am not suggesting that every neurologist should undertake research, but simply that a branch of medicine in which too few are prepared to engage in it in some relation to the urgent problems presented, and one in which young men are not being trained for it on modern lines, is doomed to sterility.

When, in 1945, the Neurology Committee of the Royal College of Physicians drew up its curriculum for the neurologist's education, it did not seriously give its mind to the need for research, to the fields of research awaiting cultivation, or the ways to fit men to work in them. It proposed, instead, a four-and-a-half year course comprising a fixed pattern of activities with no options, and no provision for the effective introduction of the aspirant to original studies. Unbelievable as it may seem, it proposed that neuro-anatomy, neurophysiology, neuropathology, biochemistry and normal psychology could all be crammed into a period of as little as six months, while, by contrast, a whole year was to be devoted to clinical psychiatry.

I find it hard to picture what was expected to emerge when, after four and a half years, this pedagogic straitjacket was peeled off the victim: surely not a man who had been trained to think independently, or had gleaned sufficient of any single scientific discipline to use it in original studies.

Happily, this neurologist, R. C. P. Pattern, Mark I, let us call him, succumbed on the committee table and never achieved embodiment, and in their 1954 report the Committee passively endorses the official specification for Mark II. His training, now grown to seven years, is to be filled by a sequence of statutory clinical appointments. The basic sciences are no longer mentioned, and the Committee confines itself to expressing the view that there should be some latitude in this scheme to allow opportunity for the study of pathology, psychiatry and surgery, and the hope that, since foreign travel and research are very important, Mark II will somehow or other find time for them.

The resolution of the committee seems to have faltered before the crucial question of where lay the authority and the responsibility, and whence was to come the enlightenment, to make possible these desirable modifications of the scheme.

This ineffectual, uninspired educational scheme stands in melancholy contrast to the thoughtful and far-sighted proposals of the Medical Research Council, and to the urgent needs of the situation. It offers no more than a seven-year tedium of largely repetitive activities calculated to damp the

spirit of any young man of original mind, or indeed of anyone who, not content to fill his days with routine tasks, asks for more from life than to obtain the economic security of consultant status.

Of course, the crux of the matter is that such a young man is aiming higher than the State or the Neurology Committee, who plan as though all that neurological medicine needs to survive and flourish is a supply of men able to meet the day-to-day needs of a State hospital and to provide consultant services.

I need not tell my listeners that I have made no serious attempt to give an account of neurology that must command an enthusiastic general assent. It would not interest me to make, nor you to listen to, a statement of this order, for it could contain no more than glimpses of the obvious.

I have aimed at a more difficult target: namely, to persuade you to contemplate seriously the tasks that lie before us in neurology: tasks that now perhaps may be more effectively tackled with the newer and more diverse applications of science now available.

I am sure that many younger neurologists feel acutely our ignorance of the nature and ætiology of many common nervous diseases, the apparent irrelevance of much neurological research to the problems of disease, and the lack of any coherent thought amongst us to give form and direction to research and theory in neurological medicine.

Surely, those who feel this must wish to see pursued by every relevant scientific discipline those studies that alone can help us to understand the processes of disease: in short to see us directing our activites to where our responsibilities as physicians so plainly rest.

Perhaps a first lesson we have to learn is that new life cannot be breathed into neurology by any scheme or committee that aims no higher than the provision of graded consultants for routine work, and a second is that the future of neurology must surely depend upon our being willing and able to maintain a living discipline that is capable of growth in every necessary mode.

Finally, we are fortunate in that in this Royal Society of Medicine we have a forum, the only one available to us, for an open discussion of the purely humane and scientific problems involved in the creation of an active and a fruitful future for neurological medicine: a discussion in which the question of our material prospects within the graded hierarchy of a State medical service will not intrude: a future in which the endeavour to understand and control disease processes will become our first aim.

Professor G. Payling Wright, D.M., F.R.C.P.:

When we attach the expression "the Future of" to any branch of medicine, we imply, I suppose, the hope and expectation that in coming years we shall acquire greater skill and success in the prevention and treatment of disease than we possess to-day. Since the prospects of any such hopes and expectations being fulfilled will depend almost wholly on our own efforts and foresight, it seems proper that from time to time we should try to take a long view of the problems before us, and see how best we can attempt their solution. The particular and more detailed lines along which our endeavours can be directed must naturally be matters of personal opinion, and need no discussion now. But certain broad considerations emerge when the progress of medicine is regarded in perspective, and it is these which seem worth the attention of those concerned with trying to guide the future of its specialities. Edmund Burke once remarked "You can never plan the future by the past". He was, I believe, mistaken, for the future and the past are a continuum. There can be no other way of directing our future efforts into productive channels except by giving close attention to the trend and progress of ideas that are shaping in our times.

As the body of medical knowledge grows and the practice of any particular branch inevitably becomes more exacting, the dangers of intellectual isolation necessarily increase. It becomes more and more difficult to maintain connexions, not only with kindred specialities but also—and it is this that may more gravely handicap progress in the long run—with the great body of the medical sciences on whose growth and prospering all aspects of medicine have depended. The "Future" of any speciality thus seems to depend importantly on two considerations: first, the extent to which it continues to acquaint itself with and assimilate contemporary discoveries in the laboratory, and second, the strength with which it can bring its influence to bear upon the increasingly large number of medical scientists—many of them unqualified medically—to induce them to undertake investigations in directions which could prove profitable to practical medicine as well as to pure science. In the past, societies which brought medical men and scientists into close and fruitful association were more numerous and influential than they are to-day; a great present need is the devising of means for re-establishing these formerly productive associations. I am sure that advances by clinicians would be warmly welcomed by many laboratory scientists—they deplore this growing isolation too.

About the middle of the last century, an anonymous French soldier coined the word "logistics". After a lapse of years, it underwent a resurrection: its popularity amongst generals in the recent war will be familiar to anyone who reads accounts of those campaigns. Napoleon's armies are said to have marched on their stomachs; Eisenhower's advanced on their "logistics". But though one can smile at this sudden verbal fashion, it should not be overlooked that the word was revived to meet a

need. It re-entered usage because the management of large bodies of men engaged in making great and rapid advances with an economy of loss required the most careful attention to their organization and supplies. In our attempts to make medical advances, "logistics" are hardly yet known. There is little organized effort to distinguish major and minor objectives through morbidity and mortality returns, to estimate whether in respect of basic knowledge we yet possess the resources needed to attain them, or to provide a personnel that is trained especially for the task itself. To take one example alone, the chronic demyelinating diseases from which nearly a thousand persons are recorded as dying every year in the United Kingdom: How many investigators in this country are seeking to unravel their pathogenesis, how much do we yet know of the chemistry of myelin and the enzymes involved in its elaboration and destruction, and how many biochemists are we encouraging to undertake what for neurology must be accepted by all as fundamental problems? My immediate purpose is to bring to your attention as earnestly as I can what seems to me to be a growing deficiency in modern medicine in *all* its branches—a failure to assess the relative importance of the many problems that confront us, to direct our attack strongly at the more serious ones, and to avoid dissipating our none too large resources of medical and scientific investigators on problems of lesser consequence.

The modern empire of medicine has expanded so rapidly that many of its frontiers are very thinly manned. It is all the more desirable, therefore, to try to persuade—for we can do no more than persuade—our scientific colleagues to be selective in the tasks to which they apply themselves. For, although it would be generally agreed that progress in medicine is intimately dependent on progress in its related sciences, this is not to infer that all advances made in the sciences are likely to prove of importance in medicine, even though we seek to leave a generous legacy to our successors a hundred years hence.

Such thoughts bring me to a consideration of the part that modern neurophysiology is taking as one of the "Institutes of Neurology"—to borrow a Scottish expression—and to ask the question, which others are more competent to answer than I, whether the time- and patron-honoured study of the biophysics of the neurone is contributing so importantly to neurology as to deserve so central a place in its councils and absorb so much of its resources, and whether physiologists might not add usefully both to science and medicine by now directing more of their attention to the vessels of the central nervous system and the cells of the neuroglia. When so noble a road has been cut into the jungle of ignorance as that planned years ago by Pflüger and du Bois-Reymond, and latterly so adorned by our countrymen at Cambridge, it becomes understandably difficult for any young physiologist to pioneer into the less well-mapped country on either hand. But should not some of them be encouraged by neurologists, who are daily confronted by the disorders of these structures, to take this enterprising step and perhaps receive some reward for doing so? Could they not be persuaded to enquire into some of the obscurities that envelop the vasculature of the central nervous system, its distinctive reaction to drugs and allergens, the peculiarities in the permeability of its capillary walls and the biophysics and biochemistry of its tissue fluids? Such problems would not only supply their own intellectual fascination—a matter of primary concern to all true scientists—but their solution could hardly fail to have beneficent repercussions, first on neuropathology—itself gravely in need of a revivifying transfusion—and later on clinical neurology itself.

If we pass to another and more youthful medical science, virology, we find a greater awareness of practical issues, though even here there is a danger that these may become subordinated to biological problems of a very fundamental order whose existence has only recently come to be appreciated. For within the lifetime of our contemporaries, no other biological science has experienced a comparable revolution either in its fundamental concepts or in its techniques of experiment. When, rather more than fifty years ago, Loeffler discovered the filter-passing agent of foot-and-mouth disease and so fathered the science of virology, he could have had no conception of the ramifications of his discovery. We are not concerned here with the theoretical issues raised by the successors of Loeffler—whether or not crystalline protein molecules which possess the power of indefinite replication and highly pathogenic properties fall within the category of the living, and what relationship they bear to the apparently sometimes comparable though usually benign cell elements we know as genes. What concerns us much more is the practical issue of the possible bearing that some of these new ideas, and the advances in technical methods which have accompanied and often engendered them, may have on neuropathology. The discoveries of latent viruses—cohabiting with unharmed cells for perhaps a lifetime—of virus pre-emption and interference and of viruses capable of provoking neoplasms when called into activity by hormones and other agents, cannot fail to have a profound influence on future ideas not only on the pathogenesis of disease but on its prevention too. This science, which began as the offshoot of bacteriology and inherited the concepts which that science had formulated, has become wholly transformed in the past twenty years and is rapidly in process of establishing its own scientific articles of faith. It may seem an overbold assertion in view of the widespread attention that has recently been directed to poliomyelitis and some other transmissible diseases whose weight falls heavily on the nervous system, but I believe that the impact of these new ideas and techniques in virus research has hardly yet fallen on neurology.

From no direction in the immediately foreseeable future does neurology seem so likely to receive an infusion of new and productive ideas as from biochemistry. The nervous tissues, and more particularly their distinctive lipoid constituents, present problems of such peculiar difficulty that most chemists have been deterred from engaging seriously in their study. One figure stands out conspicuously as a great pioneer in this field—the remarkable German surgeon Thudichum, who settled in this country after the period of reaction set in on the Continent in 1849. In his spare time, in his home-made laboratory in Kensington, Thudichum succeeded in one of the most difficult tasks that a chemist ever applied himself to—the separation, purification and constitution of the lipoids of the nervous system. His book, entitled "The Chemical Constitution of the Brains of Men and Animals", in which he brought together an account of his researches into the components of myelin, will always remain one of the classics of neurology. Unfortunately, Thudichum's achievements were not followed up with any enthusiasm by the biochemists—his techniques were arduous, his tongue had been notably caustic, and other fields seemed to offer greater likelihood of reward. To-day the acerbities and polemics that surrounded his work have been almost forgotten, and the great contributions that he made practically single-handed to neurological biochemistry are coming to be estimated more correctly.

Within the past few years, the physicists have presented the biochemists with an entirely new research instrument of unprecedented power and range of action—the isotopes of those elements of low atomic weight, hydrogen, carbon, nitrogen and others which in the aggregate form the great mass of living matter. Through the incorporation of these distinctive isotopes, substances which are chemically and biologically identical with those present in normal tissues can be introduced into the body, and their subsequent metabolism, whether of synthesis into larger structural elements or of degradation for the liberation of energy, can be followed with a surprising and gratifying exactitude. In his fascinating history of medicine, "Nosography", Knud Faber has pointed out very clearly how greatly the successive stages of its development have benefited from the assimilation of concepts and techniques from other sciences. One after another, in the past and present centuries, new ideas from outside sources have had their impact on medicine and directed its course into new and productive channels. The introduction of the physically recognizable isotopes into biochemistry has provided medicine with a technical method of wholly exceptional power for the exploration of a multitude of metabolic processes, both normal and abnormal, which formerly were far beyond its reach. These methods are now available to resume investigations into the hitherto baffling problems of the synthesis and breakdown of the brain lipoids where Thudichum and the thin ranks of his followers were compelled, through the exhaustion of their technical resources, to relinquish their task. It is encouraging to find that such interests are beginning to revive; the first international symposium on neurochemistry held at Oxford last summer may well foretoken a reanimation of this branch of neurology in this country.

It is, of course, quite impossible for me to make any instructed detailed predictions on the future of neurology as a speciality. It has seemed to me, as a general pathologist, that my most useful contribution would be to try to indicate some of the directions in which pathology and its offshoot neuropathology should try to develop if they are to keep in the main stream of scientific thought and not stagnate in its backwaters. It is the responsibility of us all to determine how this should be done. But if such efforts are to be made, they should be made *quickly*, for the connexions with these basic sciences are becoming tenuous and once lost they would be difficult to re-establish. In his book, "Human Knowledge", Bertrand Russell remarks that "speaking generally, scientific progress has been made by analysis and artificial isolation". While this statement in its explicit sense is, of course, profoundly true, implicitly it carries with it certain grave hazards. Isolation in an applied science, such as medicine, is in truth the very reverse of what is required for progress. The need is not for isolation of problems and investigators, but rather for the devising of new means, a kind of medical "logistics", that will enable a closer association and intellectual collaboration to develop between those that are daily in contact with important clinical problems and those that can bring some form of expert knowledge to help in their solution. The problems presented by patients in the clinical practice of medicine are amongst the most difficult that engage the human mind. Their solution will require all the varied scientific resources—and these are becoming increasingly powerful every year—that we can bring to bear on them. But responsibility for the initiative must necessarily lie with neurologists themselves.

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President—Sir ZACHARY COPE, M.S., M.D., F.R.C.S.

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The History of Lupus Vulgaris: Its Recognition, Nature, Treatment and Prevention

By BRIAN RUSSELL, M.D., F.R.C.P.

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ITS RECOGNITION

IN tracing back the history of lupus into the remote past, confusion inevitably arises over nomenclature. The Greeks spoke of "herpes esthiomenos", implying a creeping and corroding eruption; and the Arabic term was latinized as "formica corrosiva". Rodent ulcers, tuberculoid leprosy, and cutaneous leishmaniasis may also have been covered by these expressions.

William of Saliceto (1270) detailed the signs and course of herpes esthiomenos and Bernard de Gordon (1305) mentioned an ulcerating form of herpes which had been given the name "lupus". Dolaeus (1684) was apparently the first to define lupus as a destructive process of the face.

In the Bills of Mortality of Stuart times "cancer and wolfe" were tabulated together. The terms "cancer" and "lupus" were closely related for many years. Thus, Daniel Turner (1731) wrote: "The Cancer is a fierce and indomitable Distemper. When this Disease appearing like a small round pointed Tubercle affects the Parts of the Face and being enraged by the Application of even the mildest Medicament, it is for that Reason called Noli me tangere, or Don't meddle with me. If it seize upon the Legs and Thighs, it is termed Lupus, the Wolf, for that it is, say some, of a ravenous Nature, and like that fierce Creature, not satisfy'd but with Flesh."

Lorry (1777) recognized the identity of herpes esthiomenos with lupus. Robert Willan (1808) was the first to apply the term "lupus" exclusively to certain forms of ulceration about the face. His devoted pupil, Thomas Bateman (1829), wrote: "The term 'lupus' was intended by Dr. Willan to comprise, together with the noli me tangere affecting the nose and lips, other slow tubercular affections, especially about the face, commonly ending in ragged ulceration of the cheeks, forehead, eyelids and lips, and sometimes occurring in other parts of the body where they gradually destroy the skin and muscular parts to a considerable depth."

Rayer (1826) defined tuberculous inflammations of the skin as three in number: lupus, cancer and elephantiasis of the Greeks, and added that "perhaps Syphilitic tubercles might be added to these".

Alphée Cazenave (1842) separated noli me tangere from lupus, regarding the former as a cancerous process. He wrote: "Under the term 'noli me tangere' have been confounded lupus and cancerous affections of the face but they differ essentially from one another. Lupus seldom occurs in persons of advanced age like noli me tangere. Lupus starts with several indolent tubercles which form dry, thick scabs. Noli me tangere begins as a single tubercle with a hard circumscribed edge, lancinating pains, inflammatory swelling of the soft parts, proceeding to painful everted fungous ulcers and destroying deep-seated parts of the face. It is exasperated by caustics."

Erasmus Wilson (1857) referred to three classes of lupus, namely lupus erythematosus, lupus non-exedens, and lupus exedens, the last-named being synonymous, according to Jonathan Hutchinson (1883–84), with rodent ulcer, although it may also have been applied to ulcerated lupus, infected with cocci, or to lupus complicated by cancer.

Jonathan Hutchinson is generally credited with having been the first to describe the apple-jelly nodule—the elementary lesion of lupus, but in 1865 he wrote: "Patches of lupus often present a very peculiar tint; they are at parts glossy and semi-transparent. Mr. Wilson has well compared them to 'reddish transparent jelly effused upon the skin, and streaked with the ramifications of a few small blood vessels'. In many conditions they remind me more of a bruise in the rind of an apple than anything else. Often a patch looks a little depressed, just like a bruise or decayed spot, there being for the present no trace of tubercles."

Paul Unna described the method of examination of lupus nodules under glass pressure (diascopy).

Its Nature

Matthew Purmann (1706) listed the theories of the Ancients as to the cause of herpes esthiomenos. For example, Paraeus had regarded it as "a tumour caused by a subtle mixture of choler, phlegm, and melancholy". Purmann himself regarded lupus as "accompanied with the scurvy, an ill-cured gonorrhœa or Morbus Gallicus".

Antoine Lorry (1777) mentioned scrofula as a cause in a minority of cases. He appreciated that lupus could cause lymph stasis and elephantiasis. Pierre Rayer in 1826 pointed out that lupus especially affected scrofulous children but that it could also attack robust persons who had been in excellent health all their lives. The ulcerations of lupus were seldom successfully treated during the winter.

Tilbury Fox in 1864 held the view that "lupus has some unequivocal affinities with scrofulous caries of bone, scrofulous disease of the skin, and tuberculous ulceration of the lungs".

Jonathan Hutchinson (1865) wrote: "There can, I think, be little doubt that it is more or less connected with the tubercular diathesis. It is common in cases of lupus to find a history of phthisis in some of the patient's near relatives."

In 1881–82 Henry Leloir demonstrated the inoculability of lupus and concluded that it was a slightly virulent tuberculosis of the integument. In 1883 Robert Koch discovered tubercle bacilli in lupus, and in 1884 he inoculated a series of animals with bacilli from lupus tissue, tuberculosis resulting.

Its Treatment

From the earliest times the importance of general hygienic measures was recognized. Thus, Purmann (1706) wrote: "Cure begins with gentle Laxatives and Sudorificks. The patient must also observe a good Diet, live temperately, and observe everything the Physician or Chirurgeon directs for his Recovery."

Caustics.

Local treatment was for long limited to caustics, of which arsenic was the favourite. It was sometimes included in the guise of an adjuvant to an inert substance posing as the active principle.

In the New London Dispensatory, 1676, dedicated to King Charles II, there is a remedy savouring of "similia similibus curantur", although it precedes the birth of Samuel Hahnemann, the founder of homœopathy, by no less than eighty years. It was called "Quintessence of Wolf's Flesh" and consisted of

"℞	Wolf's flesh, newly killed ..	..	lb. x
	Mineral arsenick ..	..	lb. i
	Aron roots, dried ..	..	lb. ii
	Soot	..	lb. i *ſs*
	Lime water	..	lb. vi

It cures Cancers, and the Disease called the Wolf, as also Noli me tangere, powerfully mortifying and healing".

By the early part of the nineteenth century, the paté arsenicale de Frère Côme was widely used. Brother Jean de St. Côme (1703–1781) was a French surgeon, Jean Baseilhac, who became a monk. His paste consisted of arsenious acid, red sulphide of mercury, and burnt sponge; it was never applied to an area larger than a shilling and its use was often followed by erysipelas which, according to Cazenave, was "sometimes slight but occasionally very severe and attended by enormous swelling of the face and violent headache". Côme's paste was reserved for old and obstinate cases.

Another widely used caustic was Dupuytren's powder of 199 parts of calomel with 1 part of white oxide of arsenic. This was less powerful than Côme's paste but nevertheless an opiate often had to be administered during its use. According to Cazenave, it was "suited to slight cases of the disease, occurring in children, females, or persons of irritable habit".

In the eighteenth century another much used application was the Animal Oil of Dippel, or rectified oil of hartshorn. According to Cazenave the oil acted more as an irritant than as a caustic.

Cheaper substitutes often seem to have been used. In the Edinburgh New Dispensatory of 1816 it was stated: "If hartshorn cannot be had, the bones of any other land animal may be substituted for them."

Pierre Rayer recommended the application of one or two leeches to each tubercle, if the sufferer was not scrofulous.

Towards the end of the nineteenth century, Vienna paste came into use. It consisted of equal parts of caustic potash and quicklime in powder, with a few drops of rectified spirit and, like Canquoin's paste of equal parts of chloride of zinc and oxide of zinc, was so powerful that Balmanno Squire might well write of them: "These pastes require to be handled with great caution."

Many other substances have been used at one time or another as irritants or caustics. Bier's method of congestion was also sometimes used. The cautery has been used for treating lupus from early times but Rayer advised that it "should never be had recourse to in large ulcers of lupus on the nose. When it has been employed the bones and cartilages of the nose have been known to swell and to become attacked by chronic inflammation from which they were previously free".

In 1899 Paul Unna was using a wood spicule method in which strong mercury and carbolic lotions were twisted into the nodules on spicules and left in position, six at one session. The "patch of thorns" was covered with a mercury and carbolic plaster for two days, after which the lupus nodules were found to be converted into pustular depressions.

About the same time, Hollander's hot air treatment was introduced, in which a metal tube ¼ in. in diameter with a nozzle, was connected to a pump and a Bunsen burner. The air was heated to 300° C. The lupus tissue was described as appearing to crackle, the patch becoming blanched from ischæmia. The pain must have been intense, and ugly scarring resulted.

SURGERY.

Surgery, too, has been used from the earliest times. Bateman (1829) wrote: "By surgical means, that is by the knife, or the caustic, a separation has sometimes been made of the morbid from the sound parts, and the progress of the disease arrested."

Lang of Vienna was the chief protagonist of treatment by excision, but recurrences were common. Balmanno Squire (1888) invented a multiple linear scarifier with 17 blades in a handle ¼ in. wide which made incisions "methodically separated by interspaces sufficiently broad to avoid the risk of mortification".

The Volkmann spoon was often used for curetting out the diseased tissue; or "puncturation" in which innumerable punctures were made with the point of a lancet, and the skin minutely minced even to mortification.

IRRADIATION.

The most important advance in the treatment of lupus was the discovery by Niels Finsen of the effects of ultraviolet irradiation on lupus nodules. In 1895, Thayer had used solar rays concentrated by a powerful convex lens, but his apparatus was essentially a burning glass and Finsen in 1897 made the first report of the effects of solar irradiation with the heat rays excluded, by the interposing of a solution of ammoniacal copper sulphate between two lenses (Fig. 1). Finsen

FIG. 1.—Photograph taken before 1900. Treatment of lupus vulgaris in the London Hospital grounds by concentration of the sun's rays.

next devised an apparatus consisting of an arc lamp, a heat-extracting system, lenses for concentrating the rays, and a translucent applicator with which to express the blood from the area of skin being treated. This lamp was the outcome of four years of experimentation in which he constructed some 20 different models of arc lamps.

In the Finsen lamp the arc and the applicator had to be kept in alignment by an attendant (Fig. 2). The Finsen-Reyn lamp and a London Hospital modification of it were designed to get over these difficulties and finally the Finsen-Lomholt lamp was designed by Lomholt, head of the Finsen Institute. This lamp had the great advantage that the arc, concentration and compression systems were incorporated in one unit. Three lamps could be supervised by one attendant. Each treatment lasted half an hour, whereas Finsen lamp treatments had taken two hours.

In 1922 Reyn introduced treatment by general carbon arc irradiation as an adjunct to local Finsen treatment. Sequeira and O'Donovan found that a cure rate of about 76% with the Finsen lamp was raised to about 90% by this combined treatment, and progress was as good in winter as in summer.

Mercury vapour lamps (for example the Kromayer lamp) have not proved as effective as carbon arc lamps. They are poor emitters of the effective longer ultraviolet rays.

FIG. 2.—Photograph taken about 1903. Treatment of lupus vulgaris in the Light Department of the London Hospital by Finsen Light.

X-RAYS.

In 1901 Freund and Schiff of Vienna first used X-rays against lupus vulgaris. Sequeira reminiscing many years later wrote: "We worked on the trial and error system, little realizing the risks both operator and patient were running. All we had learned was that applications of the rays might be followed by fall of hair, for the measurement of dosage did not come into general use until about 1904. Our patient was placed about 6 in. from the tube. A ten-minute sitting was given and this was repeated daily until something happened."

In 1903 Danlos used radium and in 1939 Spiethoff reported good results from the use of Grenz rays.

TUBERCULIN.

Koch's original tuberculin (a glycerol extract of cultures of tubercle bacilli) was introduced in 1890. Its use was quickly condemned by the French school. There were alarming general reactions, even deaths, and according to Thibierge (1891) after a visit to Berlin "not a single case even apparently cured".

In 1897 Koch's new tuberculin (a glycerol-water suspension of dried and pulverized bacilli) was introduced and has been advocated by several physicians, including Morris (1904), Western (1909) and Semon and Burnell-Jones (1934). Morris thought it modified the disease process so as to make it more amenable to local treatment. Semon went so far as to recommend the establishment of special tuberculin treatment centres. As recently as 1946 Aitken thought it the remedy of choice if treatment by general ultraviolet rays was not available, and provided there was no pulmonary tuberculosis.

INTERNAL REMEDIES.

Bateman wrote: "I can mention no medicine which has been of any essential service in the cure of it."

Rayer advocated bitters and a strengthening diet and added that "if the state of the digestive organs admitted, there is sometimes benefit obtained by causing a temporary revulsion towards those parts, as by muriate of barytes or of lime". He thought tonic treatment as adapted to scrofula appeared the best to effect the resolution of the tubercles and prevent ulceration.

Arsenic was much favoured in the form of Feltz's decoction, Asiatic pills, Pearson's solution, or Fowler's solution; but Rayer wrote that "it was not until these dangerous medicaments have been administered for several months that their utility becomes manifest; they more frequently prove useless or injurious". The animal oil of Dippel was often used internally as well as externally.

Erasmus Wilson (1857) wrote: "M. Lemery, of St. Louis Hospital, had recourse to cod-liver oil, of which he speaks in the most encouraging terms. He begins with the dose of an ounce three times a day, increasing the quantity for fifteen days, by which time he reaches 6 oz. a dose. If the disease exhibit no indication of submission, he goes on until he arrives at 2 pints in the day. Should the stomach revolt, a glass or two of Seltzer water is given, and if any symptoms of derangement of the alimentary canal or fever supervene, the oil is suspended but continued again at the minimum dose as soon as the symptoms disappear." Two pints of cod-liver oil are equivalent to 100,000 units of vitamin D.

Tilbury Fox (1864) wrote: "Cod-liver oil is the sheet anchor in lupus." But Ferdinand von Hebra and Moritz Kaposi (1875) regarded it and all other internal remedies as quite inert. Lugol's iodine was sometimes given with considerable success. The Gerson diet was favoured by some. It mainly consisted of salt-free, uncooked food. Jesionek and Bernhardt (1930) developed this treatment further; the diet was rich in fresh foods of high vitamin content and this may well have accounted for much of the success that was obtained.

In 1943 Charpy in France and in 1945 Dowling and Prosser Thomas in England reported the value of calciferol (vitamin D_2) when given in massive doses. Charpy gave injections of 600,000 units once or twice a week, while Dowling and Prosser Thomas relied on oral treatment, 150,000 units being taken daily. This treatment linked up with the well-known tendency of lupus to improve in summer; with Lemery's treatment by massive dosage with cod-liver oil; and with Reyn's general carbon-arc baths.

A 50% clinical cure rate was claimed for calciferol, with improvement of most of the remainder. The histological cure rates were much lower. Vachon and Feroldi (1945) pointed out that the treatment only brought about enclosure of tuberculous foci by young connective tissue, followed by fibrosis; the foci did not disappear. Joppe (1950) obtained positive results from animal inoculation with material from clinically cleared lupus nodules. The disadvantages of calciferol treatment include its toxicity and the inadvisability of using it in pregnancy or when pulmonary tuberculosis, renal disease or hypertension coexist. Calciferol is also effective, and relatively harmless, when injected directly into the lupus nodules (Jensen, 1948). Injection of the oily vehicle alone is without effect; yet calciferol dissolved in this vehicle and injected into another part of the same nodule, causes a severe reaction, even proceeding to ulceration (Russell, 1951).

It seems that calciferol acts indirectly, by stimulating the tissues of the host to react to one of the constituents of the lipid envelope of the tubercle bacillus, possibly phthioic acid.

Van der Lugt (1952) has shown that exposure to the Finsen light increases the local concentration of vitamin D in the skin.

Calciferol has been given with streptomycin by Cornbleet (1949) and others for resistant or secondarily infected lupus. Streptomycin alone, or with para-aminosalicylic acid has not come into favour in the treatment of lupus.

The development of isoniazid is the result of years of intensive study by many workers, in particular, Chorine, Domagk, Fox, Girard, and Robitzek. Domagk (1946, 1948) found slight antituberculous activity in sulphathiazole and from this went on to develop first sulphathiadiazole which had greater activity and then an even more powerful open chain analogue, thiacetazone (p-acetylamino benzaldehyde thiosemicarbazone) designated by Domagk T B 1 or Conteben. It did not come into general use because it was often not tolerated.

In 1944–45, Chorine had found that nicotinamide possessed antituberculous bacteriostatic properties and he was able to demonstrate that it retarded the tuberculous process in guinea-pigs; isonicotinamide was found to be inactive in this respect.

In 1950, Levaditi, Girard, Vaisman and Roy combined nicotinamide with thiosemicarbazone to make the nicotinic aldehyde of thiosemicarbazone. It was shown to be effective *in vitro* and in experimental tuberculosis but it often caused digestive disturbances and was not well tolerated. Meanwhile Fox (1951) had been synthesizing and testing a large number of thiosemicarbazones. He reported that the isonicotinic aldehyde of thiosemicarbazone was superior to the nicotinic aldehyde as regards antituberculous activity. Domagk, continuing his studies, noted the remarkable activity of isonicotinic acid hydrazide. Robitzek *et al.* (1952) reported the efficacy of isonicotinic acid hydrazide in human tuberculosis and its isopropyl derivative was synthesized and found to be highly effective in a dose of 8 mg. per kg. body weight. In a dose of 300–400 mg. *per diem* (about 8 mg. per kg. body weight) which is substantially lower than the toxic level, isoniazid induces a steady involution of the nodules of lupus until after about six months there is clinical clearance. Histological clearance goes hand in hand with clinical clearance. Isonicotinic acid hydrazide acts on the tubercle bacilli in bactericidal fashion. There is no stimulation of the host's tissue reactions as with calciferol. Patients with lupus vulgaris have attenuated bacilli in the skin and they are highly resistant against pulmonary infection with tubercle bacilli, as witness the rarity of pulmonary tuberculosis in sufferers from lupus—less than 2% according to Aitken (1946). For these reasons, some dermatologists have thought it unnecessary to give other anti-tuberculous substances with isoniazid.

Meyer-Rohn and Schulz (1954) claim to have cultured virulent tubercle bacilli from excised skin of clinically healed lesions which showed on section no evidence of a tuberculous histology, from patients treated with isoniazid.

Prevention

It would not be right to conclude without paying tribute to the great success of preventive measures directed against tuberculosis, including lupus. The incidence of fresh cases of lupus attending out-patient clinics is about one-tenth of that quoted for thirty years ago.

Pasteurization of milk has probably contributed most to this reduction, some 52% of cases having been attributed to bovine tubercle bacilli in the past (Aitken, 1946). Other factors have been better nutrition, housing, clothing and hygiene; the earlier recognition of pulmonary tuberculosis; the increased use of vacuum cleaners instead of manual dusting; and cleaner methods by tattoo "artists". Present dangers, though rare, include BCG vaccination (Marcussen, 1954) and swimming baths (Hellerström, 1951; Cleveland, 1951): in some examples of cutaneous granulomata acquired from swimming baths *M. tuberculosis* has been identified but in others (Linnell and Norden, 1954)

acid-fast organisms, growing better at 30° C. and called by Swedish workers *M. balnei*, have been incriminated. The day when the townsman's skin is no longer shut off from the ultra-violet rays of the sun by the sulphurous pall of industrial and domestic smokes is yet to come.

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The History of Teething in Infancy

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THE question is often posed: Does the eruption of the milk teeth give rise to symptoms? Even to-day physicians are not unanimous in their answer to this question. Those who believe that teething may cause ill-health sometimes point out that an opinion which has been so widely held, must have arisen for some good cause. As Sir Fredric Still wrote in 1927:

"At the risk of being considered old-fashioned and unscientific, I shall mention some of the disorders to which, in my opinion, teething can give rise. I admit the difficulty of proof; we all know that coincidences are apt to be mistaken for cause and effect, but I am not inclined to disregard the accumulated experience of generations of skilled workers."

Similarly, Henoch, in his "Lectures on Children's Diseases" (1889) condemns those who "hold

that teething is a physiological process which cannot be the occasion for any morbid symptoms". He goes on to say:

"We must guard against throwing overboard the views of our medical predecessors with that presumption which has become the fashion with a section of the younger school."

The majority of our predecessors held strong views on the subject of "teething". So far from thinking it to be physiological, many even regarded it as a disease process. The gradual evolution of ideas on this subject will now be traced.

As so often happens when we begin to delve into medical history, we find that the trail leads us straight back to the ancient Greeks.

Relatively little space is devoted to children's diseases in their writings, but much of what they did write was about the evil effects of teething. There is a marked similarity between the views of Hippocrates, and the later writers, Paulus Aegineta, and others on the subject. They record the same symptoms and suggest similar treatments. Hippocrates (*c.* 440 B.C.) devotes one of his famous aphorisms (No. 25) to the subject:

"At the time of dentition there is pruritus of the gums, fever, convulsions, diarrhœa, especially when cutting the canine teeth and in those who are particularly fat and have constipated bowels."

Paulus Aegineta (*c.* 700) also wrote on dentition. He says:

"Dentition commences at about the seventh month. At that time inflammation of the gums, cheeks and tendons are apt to occur and sometimes convulsions. The child must then get nothing that required mastication and his gums should be rubbed frequently when in the bath with the finger, or soothed with the fat of fowls or the brain of a hare. When the teeth are coming through, the neck, jaws and head should be wrapped in soft wool, or they may be anointed with warm, sweet oil, some of which ought to be poured into the pores of the ears."

The coming of the Greek school of medicine was like bringing a bright lamp into a room full of guttering candles, but unfortunately the shutters of the room were not rolled back to let in the daylight of scientific medicine until many hundreds of years later.

The mediæval writers did little more than quote from the Greeks, as is well illustrated by the first textbook on pædiatrics to be published in the English language: Thomas Phayre's *Boke of Children* (1530). In his section on "Breedying of Teeth" he writes:

"About ye seveth moneth, sometime more, sometime lesse, after ye byrth, it is natural for a child to breed teeth, in which time many one is sore vexed with sodry diseases and pains, as swelling of ye gummes and jaws, unquiet crying fevers, cramps, palsies, fluxes, reumes and other infirmities, specially when it is long or ye teeth come forth, for the sooner they appear the better and the more ease it is to the childe."

The seventeenth century saw a transition between the slavish lack of criticism of the Greek school evidenced by the mediæval writers, and the beginnings of modern scientific medicine which developed, in the eighteenth century. We can fortunately obtain interesting statistical information with regard to this period from the old London Bills of Mortality. Originally published to give notice of the plague, these Bills were eventually superseded by the Registrar-General's returns in 1840. Fortunately the importance of the figures was realized by John Graunt who can lay claim to being the first statistician. Graunt (1662, p. 348) was well aware of the inaccuracy of the Bills but as he says "It is somewhat to know how many die usually before they can speak, or how many live past any assigned number of years". The reason for his doubts are obvious when we read how the figures were obtained. Graunt (1662, p. 346) records that:

"When anyone died, then, either by telling, or ringing a bell, or by bespeaking of a grave of the Sexton, the same is known to the Searchers corresponding with the same Sexton. The Searchers hereupon (who are ancient Matrons, sworn to their office) repair to the place where the dead corps lies, and by view of the same, and by other enquiries, they examine by what disease or casualty the corps died. Hereupon they make their report to the Parish Clerk."

Table I shows a few of the causes of death from the London Bills of Mortality for a period of thirty years. It will be seen that with the exception of Chrisoms and infants (Chrisoms means babies under one month—the neonatal period), teeth and worms was recorded as having been responsible for the largest number of deaths in children.

In 1689 Walter Harris published his famous *Treatise of the Acute Diseases of Infants.* Written originally in Latin, it was subsequently translated into English and fifty years later was still a standard textbook. Harris devotes considerable space to the subject of dentition which he likens to pregnancy, "the cause of innumerable calamities", which, he says, does not expose the mothers to more danger than the breeding of teeth does to their offspring. Harris advocated lancing the gum, but complained that surgeons often performed the operation inefficiently. He therefore advised that the physician make sure that the surgeon used a "more proper instrument, whether it be a pen-knife, or any other knife that has a thick blade". He thought leeches applied below each ear were of value, and advises against hot, or even warm food and drink, because of the extreme tenderness and almost burning heat of the mouth and gums. This tenderness, he says, gives rise to an obstinate refusal of all kinds of nourishment.

TABLE I.—LONDON BILLS OF MORTALITY, 1629–1660
(From Graunt, 1662)

Abortive and stillbirth ..	8,599	Impostume	1,693
Aged	15,759	King's evil	537
Ague and fever	23,784	Lunatick	158
Blasted	99	Measles	737
Bloody and scouring flux	7,818	Mother	18
Burnt and scalded ..	125	Murdered	86
Cancer	609	Overlaid	529
Sore mouth and thrush..	689	Plague	16,384
Chrisoms and infants ..	32,106	Plague in the guts ..	991
Colick and wind ..	1,389	Spotted fever	1,845
Consumption and cough	44,487	Rickets	3,681
Convulsions	9,073	Rising of the lights ..	2,700
Dropsy and tympany ..	9,623	Scurvy	593
Drowned..	827	Starved	51
Excessive drinking ..	2	Stitch	1
Executed	384	Stone and strangury ..	937
Flox and smallpox ..	10,576	Stopping of the stomach	669
French pox	392	Surfet	3,094
Frighted	21	Teeth and worms ..	14,236
Jaundice	998	Suddenly..	454

The first treatise since Hippocrates to be devoted entirely to dentition was a book by Joseph Hurlock, Surgeon, published in 1742 (Fig. 1). In the preface he quotes (1742, p. 11) Dr. Arbuthnot (1732) (Physician to Queen Anne) as saying: "above a tenth part of infants die in teething by symptoms

A
PRACTICAL TREATISE
UPON
Dentition;
OR,
The Breeding of Teeth
IN
CHILDREN:
WHEREIN
The CAUSES of the *acute Symptoms* arising in that dangerous Period are enquired into;
The REMEDIES both of the Ancients and Moderns for the *Cure* of those Evils, and the *Prevention* of their fatal Effects, are examined impartially;
Some ERRORS of Consequence corrected;
OBJECTIONS answered;
AND
A Right *Practice recommended*
UPON
OBSERVATION and EXPERIENCE.
THE WHOLE
Illustrated with proper CASES and REMARKS.

By *JOSEPH HURLOCK*, Surgeon.

Inter omnes affectus, qui circa Infantum interimuntur, nullus tot gravia Symptomata progenerat, quot DENTITIO difficilis et laboriosa.
HARRIS de Morb. Acut. Infant. *Edit. Tert. p. 78.*

LONDON:
Printed for the AUTHOR;
Sold by C. RIVINGTON, and S AUSTIN, in St. *Paul's Church-yard*; and J. HODGES against St. *Magnus* Church, *London-Bridge*, 1742

FIG. 1.—Title page of Joseph Hurlock, 1742.

proceeding from the irritation of the tender nervous parts of the jaws." The main purpose of the book is to advocate the lancing of gums as early and as often as possible. He gives many case histories including that of his own child in all of which this method of treatment was practised, and he seemed quite undeterred by the frequency of a fatal outcome.

The first man to dare to state that the eruption of teeth was not the cause of fevers, fluxes, fits and a multitude of other symptoms was William Cadogan. In 1747 he was elected a Physician to Bristol Royal Infirmary and it was while in Bristol that he wrote his "Essay upon Nursing and the Management of Children". This little book is full of practical good sense and reveals the author as a father who obviously had the welfare of children at heart. The essay was addressed to the Governors of the London Foundling Hospital and was published anonymously by them in 1748. On the subject of teething, he says:

"Breedying teeth has been thought to be, and is, fatal to many children; but I am confident that this is not from nature." Again, "Healthy children have sometimes bred their teeth without such bad attendants" (as "Fevers, fits, or other dangerous symptoms").

George Armstrong published his *Essay on Diseases most Fatal to Infants* in 1769. This was later expanded and ran to five English editions and many in German, French and Italian. In the section on the diseases associated with the eruption of teeth, he quotes Cadogan and in the main seems to agree with him. He says that "teething is said to carry off a much greater number of children than it actually does, for almost all children that die whilst they are about teeth are said to die of teething" (Armstrong, 1783).

But Cadogan's teaching did not pass uncriticized. Michael Underwood (1835), who wrote a Treatise on the diseases of children, the first edition of which was published in 1734, disagreed profoundly with Cadogan and Armstrong. He remarks scathingly:

"Some writers indeed, and particularly Dr. Cadogan and Dr. Armstrong, seem to think that teething is scarcely to be ranked among the diseases of infants."

After further discussion he concludes:

"I have therefore no doubt but that the time of dentition is most dangerous to infants and the greatest attention ought to be paid to it."

The non-medical literature of the eighteenth, as of previous centuries, is strangely lacking in references to teething in children. Rousseau (1762) suggests that children should be weaned when they cut their teeth. "This generally causes great pain and suffering." He describes how at this time they carry everything to their mouth. He suggests that it is wrong to give them hard objects such as ivory or a wolf's tooth (Fig. 2) to bite, and, by analogy with a puppy who does not practise his budding

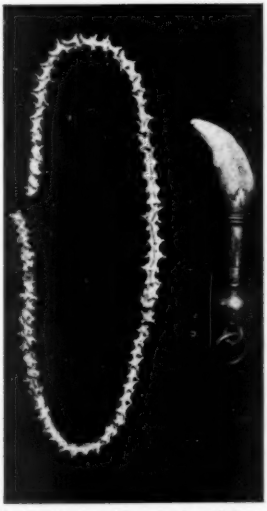

FIG. 2.—Teething necklace of viper's vertebræ, and wolf's tooth for use during dentition.
Reproduced by courtesy of Dr. T. G. H. Drake of Toronto.

teeth on pebbles, iron or bones, but on wood, leather, or rags, he suggests that the baby too should bite on soft objects "such as a small branch of a tree with leaves on".

Quacks and charlatans have always flourished, and so it is not surprising to find an advertisement in *The Times* of November 7, 1807, which reads:

"*Children Cutting Teeth.* At Mr. Burchells, Sole Proprietor and Preparer of the Anodyne Necklace to the King for the Royal Children, are sold the true original Anodyne Necklaces, after wearing of which but one night, children have immediately cut their teeth with safety, who, but just before, were on the brink of the grave with their teeth, fits, fevers, convulsions, grips, looseness etc. all proceeding from their teeth, and have almost miraculously recovered. Price 6s."

The following quotation from Hooper's Medical Dictionary of 1848 probably expresses the typical views of Victorian physicians on teething:

"Dentition is a natural process which under favourable circumstances is unattended with any symptoms which can be considered morbid; in many instances, however, it is otherwise, and disease of an alarming or even fatal character may take place."

And so, about one hundred years ago physicians had arrived at a compromise. Probably to-day few physicians would agree that "disease of a fatal character" might be the result of tooth eruption, but as recently as 1905 the Registrar-General reported that 2,343 deaths were certified as being due to teething alone (Guthrie, 1908).

Why was it that the first dentition had such an evil reputation? "Quickly tod (toothed) quickly with God" is an old Yorkshire proverb. The reason surely must be that our medical forefathers had somehow to account for the appalling infant mortality figures (*see* Table II).

TABLE II.—"INFANT MORTALITY RATES 1730–1829"—FROM LONDON BILLS OF MORTALITY (EDMONDS, 1835)

	1730–49	1750–69	1770–89	1790–1809	1810–29	1952*
Number of deaths in age group 0–2 ..	190,200	153,886	140,810	117,070	112,135	—
Total births	315,456	307,395	349,477	386,393	477,910	—
Approximate mortality per 1,000 births (computed from above figures) ..	600	500	400	300	200	28

*1952 figure refers to age group 0–1 and is included for comparison only.

Edmonds (1835) states that in the middle of the eighteenth century one-third of the total deaths for all ages occurred under the age of 2 years. A man of 90 was said to have more chance of living for a year than a newborn baby. To our forebears this decimation of young life must have appeared incomprehensible. They had no knowledge of bacterial or virus infections, no understanding of the necessity for vitamins, and their only guides in diet were a capricious appetite and economic duress. The physicians of old, learning and relearning by the tedious discipline of accumulated experience, had somehow to account for this devastatingly high infant mortality rate; and to them circumstantial evidence appeared to incriminate the eruption of teeth.

If tooth eruption was not the cause of the symptoms ascribed to it, from what diseases were these children suffering? No single condition can be named, but diarrhœa, fits and local manifestations in the mouth have been reiterated as the main symptoms of "teething" since the time of Hippocrates.

We will now consider these symptoms briefly to see whether there was any reason for their undoubted frequency if they were not in fact caused by the first dentition.

DIARRHŒA

It is, of course, obvious that the diarrhœa complained of was mainly due to infection. Cholera and dysentery abounded. Nowadays infantile diarrhœa and vomiting is very rare among breast-fed babies and it has been suggested therefore that it would have been rare in the past. But although many infants were breast fed, they were frequently fed not by their mothers but by a wet nurse. Shakespeare in "As You Like It" speaks of "the infant mewling and puking in his nurse's arms". In large towns in the eighteenth century only 3% of children were breast fed by their own mothers. These wet nurses were often of doubtful cleanliness and morality (some indeed were known as "killing nurses", who could be relied upon to "overlay" their charges). Even the best of them used to supplement the breast milk with pap or papanda. This pap was often first taken into the nurse's mouth and then squirted into the baby's mouth.

If the infants were artificially fed they fared even worse. The bottles were of primitive design and must have been impossible to keep clean. There were no rubber teats: instead a sponge was often used which must soon have become foul and a nidus of infection (Fig. 3). Asses milk was sometimes sucked by the babies direct from the udder to make sure it was not diluted. If cows milk was used it was often filthy. Smollett's (1771) appalling description of the condition of the milk sold in the streets of London is worth quoting:

"But the milk itself should not pass unanalysed—the produce of faded cabbage-leaves and sour draff, lowered with hot water, frothed with bruised snails; carried through the streets in open pails, exposed to foul rinsings discharged from doors and windows, spittle, snot and tobacco quids from foot passengers; overflowings from mud-carts, spatterings from coach-wheels; dirt and trash chuck into

FIG. 3.—Baldini's Feeding Bottle 1786.
Reproduced by courtesy of the Wellcome Historical Museum.

it by roguish boys for the joke's sake; the spewings of infants, who have slobberred in the tin-measure, which is thrown back in that condition among the milk for the benefit of the next customer; and finally the vermin that drops from the rags of the nasty drab that vends this previous mixture under the respectable denomination of milkmaid."

Thus it will be seen that breast fed or bottle fed, there was ample opportunity for babies in olden days to develop diarrhœa without incriminating teething.

CONVULSIONS

Infantile convulsions probably occurred more frequently in the past than they do to-day. This is because so many diseases which can now be prevented or cured may be ushered in by fits in children. Smallpox is an obvious example. Meningitis, too, must have been rife in the sordid slums of the cities.

Another possible cause for the convulsions was rickets which was very common before the discovery of vitamin D.

LOCAL MANIFESTATIONS

Lastly we must consider the actual condition of the mouth: the inflammation and heat of the gums (Paulus Aegineta, *c.* 700); the swelling of the jaws and gums (Metlinger, 1473; Dewees, 1826); the discharge of blood (Sylvius, 1674)—these descriptions recur again and again. What can it have been but infantile scurvy? Glisson in 1650 in his book on rickets first separated scurvy from rickets and even says "tumours do not uncommonly appear on the gums". But his teaching seems to have been forgotten, and it was not until 1878 that Dr. Cheadle, a physician to Great Ormond Street, described 3 cases of infantile scurvy. He had previously sailed to the North-West Passage with Lord Milton (Poynton, 1935) and had presumably seen adult scurvy at first hand. Of one child he says that "dark red, soft and gelatinous masses protruded from the mouth between the lips and gave the child the appearance of being engaged in sucking a piece of raw flesh". But it was left to Thomas Barlow (1883) (afterwards Sir Thomas Barlow) to give the classic description which earned for the disease the eponym of Barlow's disease.

It is of considerable interest that Joseph Hurlock (1742, p. 170) in his book on teething very nearly arrived at the correct diagnosis, for he describes an infant of 12 months who "for a good part of the summer had half a handsome chicken daily for dinner; the flesh of which was all, except the skin and sinews, constantly eat up by the child, and this liked better roasted than boiled; besides which (he had) for breakfast tea with toast and butter and about eleven a.m. some bread and butter or else broth". This diet Hurlock obviously regarded as exceptional, but more with regard to quantity

than quality. The further history of this child is of great interest. Hurlock cites him as a case of "teething" and says "the gums (were) of the deepest livid colour I have ever seen, the whole breadth of the tooth"; the child was very restless and fretful, and "the upper grinder on the right side... was turned black". In a footnote he adds, "little livid spots (were) seen afterwards in one of the arms as in the high scorbutic dyscrasia of some adults".

Apart from the similarity between the oral manifestation of teething and scurvy, it would have been almost impossible, prior to the middle of the last century, for a child in Europe to have avoided the disease at any rate in a subclinical form.

One last possibility must be considered. The symptoms of chronic mercury poisoning could easily be mistaken for "teething". Haggard (1929) remarks that, "patients with syphilis were dosed with mercury internally and rubbed with it externally until the saliva flowed from their mouths in a steady stream, their teeth were loosened and their health permanently impaired". Syphilis was well known to occur in children and doubtless they were also treated with mercury. Besides this, calomel was much used as a purgative especially in infants.

Thus for the local as well as for the general manifestation of "teething" adequate cause can be found without incriminating the actual eruption of teeth.

Diarrhœa, fever, fits, swollen bleeding gums—these were the symptoms ascribed to teething by our medical forefathers but probably few modern physicians would agree with them.

Does this mean therefore that tooth eruption causes *no* symptoms? Fortunately the answer to such a question lies outside the scope of this paper.

ACKNOWLEDGMENTS

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Section of Epidemiology and Preventive Medicine

President—A. BRADFORD HILL, C.B.E., D.Sc., Ph.D., F.R.S.

[*November* 19, 1954]

DISCUSSION ON THE ABO BLOOD GROUPS AND DISEASE

Professor Ian Aird:

Dr. Percy Stocks (1950) reported that cancer of the stomach was commoner in urban than in rural districts, commoner in the North than in the South of England. It occurred to me that this geographical distribution might be related to a racial or genetic difference which is reflected in geographical differences in the proportion of the ABO groups, group O being commoner in the North of England than in the South. We accordingly analysed (Aird *et al.*, 1953) the ABO groups in 3,632 cases of cancer of the stomach and compared them with hospital and population controls. Both in the North and in the South of England group A was substantially commoner in patients suffering from cancer of the stomach than in population and hospital controls and the same was shown in a series of 700 cases from Switzerland. Dr. Fraser Roberts showed the difference to be highly significant.

These figures contradicted the hypothesis with which the investigation had begun, for group O, which was less frequent in patients suffering from cancer of the stomach than in controls, is commonest in the North of England, where cancer of the stomach, which affects group A oftener than group O, is most common. Our figures increased the importance of Stock's geographical difference and indicated that there must be two factors operating, one presumably environmental producing the geographical difference, and the other, presumably inherited, responsible for the blood group difference. The increased frequency of A in the cancer of stomach patients must tend to reduce the degree of geographical difference of incidence of cancer of the stomach in the North and in the South of England. We subsequently (Aird *et al.*, 1954) showed a relationship between the ABO groups and peptic ulceration, a much more striking relationship indeed than that between the ABO groups and cancer. Group O occurred in 55% of 3,011 cases of peptic ulcer but only 47% of the controls, while group A occurred in 35% of the peptic ulcers and 41% of the controls. In both series, the peptic ulcers and the cancers of the stomach, group B seemed to benefit, occurring in 7·44% of the peptic ulcers as against 8·98% of the controls, and 7·76% of the cancers of the stomach as against 8·79% of the controls; these differences being highly significant.

A similar investigation applied to cancer of the colon, cancer of the bronchus and cancer of the breast revealed no statistically significant differences from the general population in the proportions of the blood groups. Table I gives a summary of the findings.

TABLE I.—A COMPARISON OF BLOOD-GROUP FREQUENCIES IN THE GENERAL POPULATION AND IN THOSE SUFFERING FROM CERTAIN DISEASES [*Brit. med. J.*, 1954, ii, 317, by kind permission]

A. Two positive results

Group	Peptic Ulcer (3,011 Cases)			Cancer of Stomach (2,745 Cases)		
	Control	Disease	% Inc. or Dec. on Control	Control	Disease	% Inc. or Dec. on Control
O	47·00	55·40	+17·9	46·78	42·95	−8·2
A	40·99	34·67	−15·4	41·38	46·19	+11·6
B	8·98	7·44	−17·1	8·79	7·76	−11·7
AB	3·03	2·49	−17·9	3·05	3·10	+1·6

B. Two negative results

Group	Cancer of Colon and Rectum (2,599 Cases)		Cancer of Bronchus (998 Cases)		Cancer of Breast (1,017 Cases)	
	Control	Disease	Control	Disease	Control	Disease
O	46·07	44·79	46·26	45·49	46·18	46·12
A	41·78	43·63	41·70	41·28	41·52	41·00
B	8·94	8·66	8·79	10·72	8·93	10·03
AB	3·21	2·92	3·25	2·51	3·36	2·85

It thus appears that either the possession of group O protects against cancer of the stomach and predisposes to peptic ulcer, or that the possession of group A predisposes to cancer of the stomach and protects against peptic ulcer. The possession of group B appears to protect against both these diseases.

If the collection of further data to explain these relationships is to be profitable it would seem desirable to consider now alternative hypotheses for the explanation of the differences which we found. The possibility that the difference can be explained by high-incidence and low-incidence genetic strains in the population in respect of these diseases can be ruled out. The association with two such different diseases of the stomach would seem to suggest that the blood group substances, mucopolysaccharides, have some direct activity in local gastric physiology and disease. In view of what is known of carcinogenesis and ulcerogenesis on the one hand, and the mucopolysaccharides on the other, it seems most unlikely that two mucopolysaccharides chemically and physically so closely similar could be responsible for the excitation, one of them of carcinoma and the other of peptic ulcer. It would be much more plausible to assume that the mucopolysaccharides in the stomach exercise a protective action, blood group O protecting particularly against carcinogenic influences and blood group A protecting particularly against ulcerogenic influences. A protective action of this kind might be more important than is suggested by the relatively small differences which we found in the proportion of blood groups. It might be, for example, that all the blood group mucopolysaccharides protect against both cancer of the stomach and peptic ulcer, but that O and B protect more effectively against cancer than A, while A and B protect more effectively against ulcer than O. This hypothesis would have the additional virtue of not conflicting with the fact that H-substance, thought once to be the blood-group mucopolysaccharide of group O, is present in the other groups as well.

Some such hypothesis as this would permit the problem to be taken into the laboratory for experimental investigation if only blood-group mucopolysaccharides were available in sufficient quantity for use in animal experiment.

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Miss A. M. Dickins (Perivale Maternity Hospital, Greenford, Middlesex):

ABO Blood Groups and Toxæmia of Pregnancy

When Dr. L. A. Pike began to investigate the relationship between the blood groups and toxæmia his first difficulty was to choose a dividing line between toxæmic and non-toxæmic patients. We chose finally to call toxæmic, patients showing any two of the following features after the 28th week of pregnancy:

A blood pressure of 140/90, albuminuria (not due to infection), or œdema.

This combination certainly constitutes toxæmia, but many milder deviations from the normal are left out. The results of this investigation, covering 3,813 consecutive admissions from March 1951 to April 1954 (Pike and Dickins, 1954), surprisingly showed a marked preponderance of group O in the 541 toxæmic patients. We had checked that the distribution of groups in our total patients was normal by comparing it with Discombe and Meyer's series of 10,000 pregnant women, and with an unpublished series also of 10,000 pregnant women, collected by Dr. J. R. E. Richardson from our own area. The correspondence was very close. Approximately the same distribution of groups was found in toxæmic patients whether they were primigravidæ or multiparæ.

Present material and results.—In the published series patients had been included whose blood pressure reached 140/90 in labour only, whose systolic or diastolic only reached or exceeded the appropriate level, without the other necessarily reaching it, and some who gave a history of toxæmia in a past pregnancy which seemed probable, but was not proved. To satisfy myself that the peculiar difference shown persisted, however strict the criteria, I have now excluded the patients just mentioned, and have extended the series, with Dr. Richardson's help, to include 4,245 consecutive admissions. 117 cases have had to be discarded because of abortions, or inadequate notes. The distribution of groups again agrees well with Discombe and Meyer's (1952) and Richardson's unpublished series.

TABLE I.—COMPARISON OF BLOOD-GROUP FREQUENCIES IN THE GENERAL POPULATION, NON-TOXÆMIC, AND TOXÆMIC PATIENTS

Group	All patients	Non-toxæmic patients	Toxæmic patients	% increase or decrease of toxæmic patients over non-toxæmic patients
O	46·4%	45·7%	51·7%	+13
A	42·5%	43·1%	38·2%	−11
B	8·2%	8·3%	7·1%	−14
AB	3·0%	2·9%	3·0%	+ 3
Totals	4,128	3,623	505	

The toxæmic patients show again an increase in group O. Comparing the relative proportions of group O and the other groups taken together, for toxæmic and non-toxæmic patients, χ^2 is 6·4 which corresponds to a probability of a little more than 1/100 of so great a deviation occurring by chance. The corresponding χ^2 in the first series was 11·7. The drop is disturbing and we hope that the findings will be confirmed by others, before being taken as typical. A greater contribution to the difference now appears to be made by the multiparæ, who show 56·8% group O compared with 50% group O in primigravidæ.

I have attempted to divide the toxæmic patients into those with essential hypertension in pregnancy and those with a true pre-eclamptic toxæmia of pregnancy. As the pre-pregnant levels are rarely available, to make this distinction one usually studies the blood pressure before the 20th week of pregnancy, when if anything it will be lower than the patient's normal. A common dividing line at this stage is 120/80. This was adopted by Professor F. J. Browne after Robinson and Brucer's paper in 1940, and receives some support from Hamilton *et al.* (1954). Their tables show that an average diastolic pressure of 80 is not expected even in non-pregnant women until the age group 35–42. The average age of all our toxæmic patients is 28·6.

TABLE II.—COMPARISON OF BLOOD-GROUP FREQUENCIES IN PATIENTS WITH PRE-ECLAMPTIC TOXÆMIA OF PREGNANCY AND PATIENTS WITH ESSENTIAL HYPERTENSION IN PREGNANCY

Group	Pre-eclamptic toxæmia	Essential hypertension	Unclassifiable
O	50·6%	52·3%	54·8%
A	40·2%	36·0%	35·5%
B	7·0%	7·6%	6·5%
AB	2·2%	4·1%	3·2%
Totals	271	172	62

As far as these rather inadequate figures go, the increase in Group O appears to be shared equally by the two categories of patient.

DISCUSSION

Boorman, Daley and Dodd in 1947, in their survey of 2,000 women, were taking albuminuria as an essential criterion for toxæmia, so had only 83 whom they regarded as toxæmic. They state that the blood group distribution was normal, but do not give the figures in detail. If, however, a preponderance of group O in toxæmic patients proves typical some explanation must be sought. The association might be explained in some way by ABO incompatibility between fœtus and mother. This is a rather attractive hypothesis as the pathological features of the disease might then possibly be explained by an antigen-antibody reaction in the smaller blood vessels. Iso-immunization of the mother can take place during a heterospecific pregnancy (that is, a pregnancy in which the fœtus bears a blood group antigen of the ABO system absent from the maternal red cells). Group O mothers are much more likely than others to have a heterospecific pregnancy. Harvey Smith in 1945 found that a rise in titre in the mother was only shown when the babies were secretors of group-specific substance and that it persisted or increased in the puerperium. Here at last might have been a mechanism explaining post-partum eclampsia. He did not, however, mention the clinical condition of his patients. Dienst in 1905 stated categorically that "eclampsia is nothing but a transfusion of incompatible blood of the fœtus into the mother's circulation as a result of a communication between the two". He found a rising antibody titre during the puerperium in eclamptics, and thought that he could demonstrate deficiencies in toxæmic placentæ. McQuarrie (1923) and Edlén *et al.* (1947), supported this view, but Dienst (1908), Allen (1926) and Hurst, Taylor and Wiener (1946) found no increase in heterospecific pregnancies in toxæmic women. None of these papers define toxæmia, and the numbers are small.

The suggestion in my figures that the increase in group O is shared equally between those ultimately toxæmic women starting pregnancy with essential hypertension (usually mild) and those starting with a normal blood pressure is, in a sense, disappointing. It suggests that we have not been investigating a difference peculiar to pregnancy, and that it may not be profitable to search for a cause of the relationship limited to the conditions obtaining in pregnancy. Browne and Dodds in 1939 when studying the remote prognosis of toxæmia of pregnancy found that 51% of their patients developed residual hypertension. They concluded that these patients "have a familial tendency to the disease which pregnancy has merely revealed, and the onset of which the pregnancy has hastened". Isenhour, Kuder, and Dill in 1942 found no difference in diastolic blood pressure between parous and nulliparous women and concluded that residual hypertension could not be caused by toxæmia. It seems likely that toxæmic women are, in fact, part of the general hypertensive population and we must now await blood-group studies in non-pregnant hypertensives.

But what could connect a high incidence of group O and a tendency to hypertension? Could it be a direct effect of group O specific substance on the blood vessels, or an absence of protection by

group A or B specific substances? An annotation in the *British Medical Journal* (1954) recalled the work of Bussard and Eyquem in 1947 who showed an immunological relationship between human chorionic gonadotrophins and group A specific substance. The annotation also quoted Professor Rimington (1954), who tells me that he found a chemical similarity between the two substances, which he still believes to exist.

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Dr. J. R. E. Richardson (Department of Pathology, King Edward Memorial Hospital, Ealing):

ABO Blood Groups and Toxæmia of Pregnancy

It has been suggested that the number of heterospecific pregnancies occurring in a group of toxæmic mothers may differ from that occurring in the normal population.

The definition of heterospecific frequency used is the same as that used by Pike and Dickins (1954), namely:

A pregnancy in which the fœtus carries an ABO group antigen absent from the maternal blood cells.

Compared with a normal population twice the number of heterospecific pregnancies would be necessary to account for the difference in blood group frequency between the two sets of figures in Miss Dickins' Table I (p. 140).

The figures used in this analysis are: Firstly, 56 D.—negative toxæmic mothers in which the group of the infant was determined and secondly, all the 21 cases of toxæmia occurring in Perivale Hospital since October 1, 1954.

The blood groups of the 77 mothers are shown in Table I.

TABLE I.—BLOOD GROUPS OF TOXÆMIC MOTHERS WHOSE INFANTS HAVE BEEN TESTED

Group O	Group A	Group B	Group AB	Total
51	19	4	3	77

In this sample there is a marked increase in the number of group O pregnancies but the only explanation that can be offered for this is one due to chance, as no other can be suggested.

The expected number of homo- and hetero-specific pregnancies may be calculated from the gene frequencies of the normal population for this particular sample in Table I and are shown in Table III.

The heterospecific population in Tables II and III may be combined to show the observed and expected figures for this series in Table IV.

TABLE II.—OBSERVED HOMOSPECIFIC AND HETEROSPECIFIC PREGNANCIES OCCURRING IN MOTHERS FROM TABLE I

	Homospecific	Heterospecific	Total
All groups	57	20	77
Group O	33	18	51

TABLE III.—EXPECTED NUMBER OF HOMOSPECIFIC AND HETEROSPECIFIC PREGNANCIES IF THE GENOTYPES HAD BEEN THOSE OF THE NORMAL POPULATION (IN MISS DICKINS' TABLE I, p. 140)

	Homospecific	Heterospecific	Total
All groups	58·3	18·7	77·0
Group O	34·5	16·5	51·0

TABLE IV.—COMBINING TABLES II and III FOR HETEROSPECIFIC PREGNANCIES

	Expected	Observed
All groups	18·7	20
Group O	16·5	18

It is impossible for this small sample to do more than indicate a trend but the figures are suggestive that the number of heterospecific pregnancies in toxæmic women is not in excess of that found in a normal population and it is most unlikely that heterospecific pregnancies would account for the preponderance of Group O found by Pike and Dickins.

It will require an extended series before anything approaching statistical significance is demonstrated.

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Dr. J. A. **Fraser Roberts** (Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine):

The Biometrical Approach

The discovery of definite associations between the ABO blood groups and disease, apart from certain antigenic phenomena, is very recent. To use an analogy, it has just been found that cholera has something to do with the water supply. We are at that earliest stage when epidemiological methods, using the term in a wide sense, make some of their most valuable contributions by directing attention to the existence of problems and suggesting profitable lines for future research. For my part in this Discussion, I should like to direct attention to some of the epidemiological or biometric aspects.

The first stage of all is the search for possible associations between blood-group frequencies and particular diseases. We have, at present, little or no inkling as to whether associations are likely to exist or not. We have to proceed quite empirically. In view of recent experience one would be disinclined to say that it was not worth while studying blood-group frequencies in any disease; though the qualification must be added that in view of the numbers required they must at present be common diseases. One important requirement is that the criteria for including cases in the series should be very rigidly and precisely defined. Three reasons can be given for this. First, we are less likely to miss an association owing to heterogeneity of the material. Secondly, for reasonably quick results we must rely on existing records, and only if the criteria are precise can the difficult task of extracting the information be carried out satisfactorily. Thirdly, it is most important to be able to add series which are individually too small for analysis and also to compare results from different parts of the world; so we must know that we are all talking about the same thing before we can go on to compare and combine our figures.

Once an association has been established many lines of work present themselves, but we must first be reasonably sure that an association does, in fact, exist. Otherwise a great deal of time and effort will be wasted. There is no need to be hypnotized by conventional levels of significance, however useful these arbitrary limits may be with a wide variety of problems. We are fully entitled to adopt any level of significance we like in the light of what seems appropriate to the problem in hand. With associations between blood groups and disease I would suggest that we ought to demand a really high level of significance. Personally, I should not feel happy unless the probability that the observed associations could be due to chance falls to less than one in a thousand. Short of this it is better to regard an apparent difference, however suggestive, only as an indication for the collection of more data. Some reasons should, perhaps, be given for this choice. First, we have no ancillary evidence; the association stands or falls simply on the figures themselves. Secondly, large numbers of studies are going on and some significant differences are sure to turn up by chance—in fact, of course, on the average once in 20 times at the 5% level and once in a hundred times at the 1% level. Thirdly, excellent though the control samples for frequencies in the general population may be, there is a margin for error. The disease series may not correspond precisely to the control sample chosen for comparison, so that sometimes a difference may be somewhat exaggerated. (Actually a very small difference, even though significant, might be suspect. But numbers adequate for testing very small differences are not likely to be produced for a long time to come.) Finally, though this may sound like weakness, one cannot avoid a fear that perhaps there may be some quite unsuspected factors disturbing the comparison and one would like to leave a margin of safety for these hypothetical dangers also.

For a few conditions an association has been established at well below the one in a thousand level of probability, and so we can go further. First of all, there is subdivision. Is the excess of persons of group O, or of group A, or whatever it may be, the same in men and women? Is there any indication of age-differences? Is there any difference between subdivisions of the disease? Here it seems justifiable to turn to a different order of probabilities in determining what we choose to call significant. If we had found in peptic ulcer, for example, which we did not, that there was a difference between men and women, and if that difference attained significance at the 5% level, we would say that we had good evidence that there was a real sex difference. We are, in fact, back again in the region where ordinary conventional levels of significance seem useful and appropriate.

We know most about the association with peptic ulcer, and here the results of subdivision are rather striking. There is no indication of any difference between men and women, nor does the

age distribution of patients of group O, which is heavily in excess, differ from the age distribution of patients belonging to the other groups. The patients with duodenal ulcer in our series show a bigger excess of O than those with gastric ulcer, but it is not significant at the 5% level. Nevertheless, it is large enough to make it desirable to collect more figures.

Subdivision, then, has so far revealed no differences and this points to what might be a profitable further step to take. This is to enlarge the definition. It would be very interesting to see whether the excess of O extends to less certain ulcers and to dyspepsias without ulcers. This probably entails work by a team on new patients—not just on records—with a classification of signs and symptoms and including such things, for example, as assessment of hyperchlorhydria. It is, of course, the sort of investigation that would not be worth while until the basic primary association had been established. The numbers needed would, as always, be large—say not less than 1,000—but it should not be unmanageably large with so common a condition.

Already we can draw some deductions. Peptic ulcer is a disease which fluctuates greatly in incidence over relatively short periods of time. It is a disease with psychological associations. It would be rather queer if it was the actual presence of an ulcer which was associated with belonging to blood group O. It is much more likely that the association depends on some predisposing factor, which is present whether the ulcer actually develops or not. The lack of sex and age differences supports this view. In spite of the very large difference in sex incidence, especially in duodenal ulcer, in spite of the many differences between duodenal and gastric ulcer, the picture we see is an overall increased frequency of persons of group O, which is proportionately the same in both sexes and over all ages. There may be some analogy here with certain industrial cancers, in which, though the incidence is greatly raised owing to the exposure to some carcinogen, it is found to be a rise over all ages.

There is the same sort of suggestion in the results Miss Dickins has shown on toxæmia of pregnancy. The proportion of women of group O is raised both in those with essential hypertension and those with pre-eclamptic toxæmia. It seems likely that both in peptic ulcer and in toxæmia of pregnancy it is some general background factors that we should search for.

I might end with a word on yet a third level at which biometric method can be helpful. The first level was the preliminary establishment of an association, involving tests of significance for which we demand low levels of probability. The next level also involves tests of significance, though used in more variety and with more flexibility. The third level is that of estimation. It will become important not merely to know that a difference exists, but also to estimate how big it is, and what are the limits of error of that estimate. This may be needed when there is a hypothesis to test. If a particular factor were responsible for an association, is that consistent with the actual amount of the difference? Already there are indications that this stage is being reached. Dr. Richardson has given an interesting example, involving a preliminary test as to whether it is possible on a particular hypothesis to account for the observed excess of women of group O in patients suffering from toxæmia of pregnancy.

So I will end where I began. We are fortunate in seeing, from its earliest stages, an example of how the epidemiological and biometrical approach can disclose new problems and then direct attention to profitable lines for researches of various kinds. And I think that we are all the more pleased because we recognize clearly that epidemiology is the beginning and not the end of advances in knowledge.